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Liens entre l'histoire obstétrique, les facteurs de risque nutritionnels et génétiques, la santé mentale périnatale et la durée de la gestation

par

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Résumé

Problématique : La période périnatale est critique pour la santé et le développement de l'enfant. Les problèmes de santé mentale pendant la grossesse et après l'accouchement peuvent mener à des conséquences néfastes sur le développement de l'enfant et les issues plus tardives de sa santé. Cette thèse se concentre sur deux problèmes de santé mentale périnatale d'intérêt substantiel : le stress psychosocial pendant la grossesse et la dépression postnatale.

Méthodes : Dans la première partie, nous donnons un aperçu de la dépression postnatale et effectuons une revue de la littérature portant sur deux facteurs de risque qui suscitent un nouvel intérêt, soit le génotype du transporteur de la sérotonine et l'état des acides gras oméga-3 polyinsaturés. Ensuite, dans le cadre de la deuxième partie, nous effectuons une revue de la littérature sur le stress psychosocial pendant la grossesse et la naissance prématurée, le tout en discutant les mécanismes physiologiques reliant ces deux derniers. Puis, nous examinons les liens existant entre le stress psychosocial et la durée de gestation au sein de la cohorte 3D, une étude longitudinale réalisée au Québec. Pour conclure, nous effectuons une investigation plus détaillée sur les facteurs de risque de l'anxiété liée à la grossesse dans la cohorte 3D, ceci en mettant l'accent sur l'historique des grossesses antérieures.

Résultats : Dans la première partie, trois études menées rigoureusement révèlent des associations entre le génotype du transporteur de la sérotonine et la dépression postnatale. De même, les preuves s'accumulent à l'effet qu'une insuffisance en acides gras oméga-3 polyinsaturés soit associée à un risque plus élevé de dépression postnatale. Des données probantes préliminaires suggèrent qu'il pourrait y avoir une interaction entre les deux nouveaux facteurs de risque.

Dans la deuxième partie, la littérature montre des liens entre le stress psychosocial pendant la grossesse et la naissance prématurée qui varient selon les dimensions du stress et le moment de mesure de celui-ci. Des associations plus fortes sont généralement trouvées plus tôt durant la gestation, alors que la perception subjective du stress et l'anxiété liée à la grossesse sont les plus étroitement associées à la naissance prématurée. Les voies comportementales, infectieuses, neuroinflammatoires, et neuroendocriniennes sont identifiées comme mécanismes physiologiques potentiels. Dans notre étude sur le stress psychosocial et la durée de la gestation au sein la cohorte 3D, nous avons observé une faible association entre l'anxiété liée à la grossesse au troisième trimestre et la naissance spontanée avant 39 semaines de gestation. Dans notre étude sur l'histoire obstétrique et l'anxiété liée à la grossesse, des

liens indépendants ont été observés entre plusieurs issues de grossesses antérieures et l'anxiété liée à une grossesse subséquente.

Conclusions : Les données probantes de la première partie soutiennent un programme de recherche ayant pour but de clarifier les liens entre les acides gras oméga-3 polyinsaturés, le génotype du transporteur de la sérotonine et la dépression postnatale. Dans la deuxième partie, nos résultats mettent en lumière l'importance relative du stress psychosocial comme prédicteur de la durée de gestation, tout en faisant une contribution importante pour des méta-analyses futures. Ils suggèrent d'ailleurs de nouvelles pistes de recherche pour les cadres conceptuels liant le stress et les issues de la naissance.

Mots clés : santé périnatale, santé mentale, accouchement prématuré, dépression postnatale, stress psychosocial

Abstract

Background: The perinatal period is a foundation period for health and development. Mental health problems during pregnancy and after childbirth can have adverse consequences on child development and later health outcomes. This thesis focuses on two perinatal mental health problems of substantial interest: psychosocial stress during pregnancy and postpartum depression.

Methods: For the first section, we provide an overview of postpartum depression and review the literature on two risk factors of emerging interest: serotonin transporter genotype and omega-3 polyunsaturated fatty acid status. For the second section, we review the literature on psychosocial stress during pregnancy and preterm birth, discussing physiologic mechanisms linking the two. This is followed by an investigation of the associations between psychosocial stress during pregnancy and length of gestation in the 3D Study, a longitudinal birth cohort in Québec. Finally, we conduct a more detailed investigation of the antecedents of pregnancy anxiety, focusing on previous pregnancy outcomes in the 3D cohort.

Results: For the first section, three carefully conducted studies reported associations between serotonin transporter genotype and postpartum depression. Accumulating evidence also suggests inadequate intake of omega-3 fatty acids to be associated with elevated postpartum depression risk. Preliminary data suggest there could be an interaction between these two emerging risk factors.

For the second section, associations found in the literature between psychosocial stress in pregnancy and preterm birth varied according to the dimensions and timing of stress. Stronger associations were generally found in early pregnancy, and subjective perception of stress and pregnancy anxiety were the stress measures most closely associated with preterm birth. Potential physiologic pathways identified include behavioural, infectious, neuroinflammatory, and neuroendocrine mechanisms. In our investigation of psychosocial stress and length of gestation in the 3D cohort, we observed an association of small magnitude between pregnancy anxiety in the third trimester and spontaneous birth before 39 weeks. In our study of predictors of pregnancy anxiety, independent associations were found between several previous pregnancy outcomes and pregnancy anxiety in a subsequent pregnancy.

Conclusions: Results from the first section support a research agenda clarifying the associations between omega-3 fatty acids, serotonin transporter genotype, and postpartum depression. Findings from the second section shed light on the relative importance of psychosocial stress as a predictor of

pregnancy duration while making an important contribution for future meta-analyses on this topic. Our results also suggest future directions for conceptual frameworks linking stress and birth outcomes.

Keywords: perinatal health, mental health, preterm birth, postpartum depression, psychosocial stress

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Liste des abréviations

5-HT : serotonin

5-HTT : serotonin transporter

5-HTTLPR : serotonin transporter gene linked polymorphic region

AD : antidepressant

BDI : Beck Depression Inventory

CAP : cholinergic anti-inflammatory pathway

CÉR : comité d'éthique de la recherche

CES-D : Center for Epidemiological Studies Depression Scale

CRH : corticotropin-releasing hormone

DHA : docosahexaenoic acid

DPN : dépression postnatale

ECG : electrocardiogram

ECMS : Enquête canadienne sur les mesures de la santé

EPA : eicosapentaenoic acid

EPDS : Edinburgh Postnatal Depression Scale

fMRI : functional magnetic resonance imaging

HPA : hypothalamic-pituitary-adrenal

HRV : heart rate variability

IL : interleukin

ISRS : inhibiteur sélectif de la recapture de la sérotonine

MDD : major depressive disorder

n-3 PUFA : acide gras oméga-3 polyinsaturé, omega-3 polyunsaturated fatty acid

NP : naissance prématurée

PDQ : Prenatal Distress Questionnaire

PDSS : Postpartum Depression Screening Scale

PET : positron emission tomography

PFC : prefrontal cortex

PPD : postpartum depression

PSP : psychosocial stress during pregnancy

PSS : Perceived Stress Scale

PTB : preterm birth

QMI : Quality Marriage Index

RPM : rupture prématurée des membranes

SERT : génotype du transporteur de la sérotonine

SES : socioeconomic status

SPG : stress psychosocial pendant la grossesse

TNF : tumor necrosis factor

VFC : variabilité de fréquence cardiaque

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Chapitre 1

La santé mentale périnatale : l'intersection de deux aspects critiques de la santé

Introduction

Une grossesse et un accouchement en bonne santé sont critiques pour que l'enfant puisse commencer sa vie de la meilleure façon possible. Les problèmes de santé mentale de la mère pendant la grossesse et après l'accouchement peuvent mener à des conséquences néfastes sur le développement de l'enfant et peuvent même avoir des effets à long terme sur sa santé. Cette thèse porte sur deux problèmes importants de santé mentale maternelle périnatale : la dépression postnatale (DPN) et le stress psychosocial pendant la grossesse (SPG).

La santé mentale périnatale

Le mot « périnatal » vient du grec *peri*, signifiant « près », et du latin *nasci*, signifiant « naître ». Les limites précises de la période périnatale varient selon les définitions, mais pour les buts de la recherche en santé, celles-ci s'étendent du moment de la conception jusqu'à la fin de la première année après l'accouchement [1].

La période périnatale est unique du point de vue de la santé mentale. La grossesse, l'accouchement et la responsabilité des soins pour un (ou plusieurs) nouveau-né(s) impliquent des facteurs de stress et des exigences exceptionnelles de la part des femmes, ainsi que de leur partenaire et de leur famille élargie [2, 3]. Il n'est donc pas surprenant que des problèmes de comportement et d'humeur puissent survenir chez les femmes enceintes ou chez celles qui viennent d'accoucher. Durant la période périnatale, non seulement le risque de développer des problèmes de santé mentale est plus élevé, mais la sévérité, la durée et les conséquences de ces maladies peuvent également être plus

sérieuses [4, 5]. De plus, un certain nombre de femmes sont réticentes à la prise de médicaments psychotropes durant cette période à cause de leurs inquiétudes vis-à-vis des effets nocifs sur leurs enfants [6-10]. Enfin, un nouvel axe de recherches démontre comment des problèmes en santé mentale pendant la période périnatale peuvent avoir des conséquences sur la santé de la progéniture à l'âge adulte, voire sur les générations suivantes [11-13].

Enjeux pendant la grossesse

Aux changements hormonaux et corporels accompagnant une grossesse, les troubles de la santé mentale peuvent ajouter des difficultés supplémentaires chez les femmes enceintes. Des problèmes comme le stress, l'anxiété et la dépression peuvent se manifester avec divers degrés de sévérité. Des diagnostics psychiatriques plus graves comme les troubles d'anxiété cliniques, la bipolarité et la psychose peuvent avoir des effets graves sur une femme et son enfant [14].

Le stress et l'anxiété. Le stress et l'anxiété vécus par une mère sont des éléments clés de la santé mentale périnatale. Le stress maternel pendant la grossesse est associé avec divers effets néfastes sur la mère et l'enfant. On trouve que le stress conduit au travail et à l'accouchement prématurés par la sécrétion d'ocytocine et de prostaglandines [15]. Des connaissances de modèles animaux suggèrent également des effets du stress maternel sur le fœtus pouvant nuire au développement fœtal. En effet, le stress maternel peut limiter l'oxygène et les nutriments disponibles à cause de l'augmentation du taux de catécholamines [16], et le système nerveux central fœtal peut également être compromis via les hormones surrénales [17]. Enfin, les changements épigénétiques placentaires provenant du stress maternel peuvent augmenter le risque de développer des maladies d'adulte chez le fœtus [18].

À la lumière de ces hypothèses concernant les effets du stress maternel sur le développement fœtal, il n'est pas surprenant que des liens aient été établis entre les évènements extrêmes pendant la grossesse, comme les désastres naturels, et les issues de la grossesse et le développement de l'enfant [19]. Par exemple, un groupe de femmes ayant vécu un tremblement de terre en Californie pendant le

premier trimestre de leur grossesse avaient une durée de gestation plus d'une semaine plus courte que les sujets de contrôle ayant déjà accouché au moment du tremblement de terre [20]. Une étude sur un groupe de femmes enceintes lors du passage de l'ouragan Katrina a indiqué que les mères ayant vécu les expériences les plus sévères correspondaient à un taux élevé d'accouchements prématurés et que leur bébé avait un poids faible à la naissance [21]. Au Québec, la tempête du grand verglas de 1998 a fourni une expérience dans les conditions naturelles pour étudier les effets du stress aigu prénatal sur les issues de grossesse et sur le développement de l'enfant [22, 23]. Une série d'études suivant cet évènement sur une période de plus de 10 ans a démontré que des liens existaient entre l'exposition prénatale au stress lié à la tempête et divers troubles de santé de l'enfant, notamment la durée de la gestation [24], la naissance prématurée (NP) [25], la sécrétion d'insuline [26], l'obésité [27], la fonction linguistique[28, 29] et motrice [30], l'asthme [31], les traits d'autisme [32], et la methylation des gènes liés à la fonction immunitaire [33].

Cette thèse explore les prédicteurs et les séquelles de plusieurs formes de stress psychosocial pendant la grossesse, en mettant l'accent sur l'anxiété liée à la grossesse. Les chapitres 3 et 4 en particulier examinent les liens entre le stress psychosocial pendant la grossesse et la NP. Le chapitre 5, quant à lui, se penche sur les prédicteurs obstétriques de l'anxiété liée à la grossesse, afin notamment d'explorer de façon plus large pour quelle raison cette mesure semble être un facteur tellement utile pour prévoir les issues de l'accouchement.

La dépression. La dépression clinique, un autre élément clé de la santé mentale maternelle périnatale, est une condition psychiatrique qui va au-delà de la tristesse ou de la mélancolie. Elle est définie en termes de ses symptômes. Selon le *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*, produit par l'*American Psychiatric Association*, au moins cinq symptômes sont nécessaires parmi ceux suivants, et ce, pendant une durée d'au moins deux semaines, pour former un diagnostic : une perte d'intérêt, une humeur dépressive, une perturbation de l'appétit ou du poids, une

perturbation du sommeil, un changement psychomoteur, une perte d'énergie, des sentiments de culpabilité ou de manque d'estime de soi, des difficultés de concentration ou à prendre des décisions, ainsi que des pensées morbides ou suicidaires [34]. Dans la recherche et la pratique clinique, les symptômes dépressifs sont souvent mesurés à l'aide d'échelles de dépistage écrites, avec la possibilité d'un suivi sous forme d'entrevue clinique structurée pour ceux et celles ayant un dépistage positif. Au-delà de l'utilité de cette procédure pour permettre de poser des diagnostics individuels, cette approche en deux étapes est utile dans l'estimation de la prévalence populationnelle de la dépression, notamment dans le cadre de projets de recherche ou de planification de santé publique.

La neurobiologie de la dépression. À la suite de cette définition axée sur les symptômes, un nombre croissant de publications sur le sujet ont éclairé la neurobiologie qui sous-tend la dépression. Les patients souffrant de dépression font preuve d'un niveau élevé d'activité dans les régions cérébrales qui contrôlent la régulation de l'humeur, la mémoire, la douleur, l'agressivité, l'estimation du risque et l'attention [35]. La grosseur de certaines régions du cerveau est également affectée. Par exemple, l'hippocampe des patients dépressifs est réduit de volume [36], et ce, de manière proportionnelle à la sévérité et à la durée de la maladie [37]. Chez les enfants, la taille de l'amygdale, le système d'alarme du cerveau, est reliée aux symptômes de dépression de leurs mères depuis la naissance [38].

Des changements hormonaux sont également observés chez les patients souffrant de dépression. En comparaison avec les sujets contrôles, les patients dépressifs ont un niveau plus élevé de cortisol, une des hormones du stress. Par ailleurs, le taux de glucocorticoïdes est également élevé, et leurs récepteurs deviennent moins sensibles pendant un état de dépression, ce qui rend l'individu plus vulnérable et sensible au stress [35]. Finalement, une déficience en monoamines, comme la sérotonine, la noradrénaline et la dopamine, est aussi impliquée dans la pathogenèse de la dépression [39-41]. Ces neurotransmetteurs sont donc ciblés par des médicaments antidépresseurs de type inhibiteur sélectif de la recapture de la sérotonine (ISRS) [42].

La dépression prénatale. On estime qu'entre 10 % et 25 % des femmes enceintes vivent une dépression pendant la grossesse [43]. Les conséquences potentielles sont nombreuses et incluent des complications de la grossesse comme la pré-éclampsie et l'avortement spontané [44, 45], la NP et le faible poids de naissance [46, 47], ainsi que des effets sur le développement de l'enfant [48]. Le dépistage de la dépression pendant la grossesse est confondu par le fait que certains symptômes de la dépression, tels que la fatigue et les changements liés au sommeil ou à l'appétit, peuvent être difficiles à distinguer des traits d'une grossesse normale. Par conséquent, une entrevue clinique structurée constitue la norme par excellence pour le diagnostic de la dépression prénatale. Plusieurs instruments validés sont utilisés pour le dépistage de la dépression périnatale, y compris le *Beck Depression Inventory* (BDI) [49], le *Center for Epidemiological Studies Depression Scale* (CES-D) [50], l'*Edinburgh Postnatal Depression Scale* (EPDS) [51], et le *Postpartum Depression Screening Scale* (PDSS) [52]. Dans le contexte de la recherche , les résultats de ces instruments sont analysés soit de façon continue (par exemple, en comparant les scores moyens entre deux groupes de participants dans une étude), soit de façon dichotomisée (en examinant le pourcentage des scores au-dessus d'un seuil prédéterminé) [43, 53, 54].

Les enjeux après l'accouchement

L'arrivée d'un enfant est souvent une occasion heureuse, mais elle peut aussi être accompagnée de difficultés [55]. Les changements hormonaux de l'accouchement ainsi que la responsabilité de répondre aux besoins de l'enfant peuvent susciter ou exacerber des troubles de santé mentale pendant la période postnatale [56].

Les *postpartum blues.* Le terme *postpartum blues* ou *baby blues* réfère à une réaction dépressive légère et non-spécifique pendant les jours suivant l'accouchement. Il est principalement lié à des changements hormonaux. Les symptômes des *postpartum blues* incluent les crises de larmes,

l'irritabilité, l'anxiété, l'hypochondrie et l'insomnie. La prévalence est estimée entre 15 % et 84 %, dépendamment des critères de la définition de cas, le moment et la fréquence de la mesure [53, 57, 58].

La dépression postnatale. L'*American College of Obstetricians and Gynecologists* décrit la dépression postnatale (DPN) comme la complication obstétrique la moins reconnue, la plus sous-diagnostiquée et sous-traitée aux États-Unis [59]. La prévalence de la DPN y est estimée entre 10 % et 15 % [60, 61]. Comme c'est le cas pour la dépression prénatale, il peut être difficile de détecter les différences entre la DPN et les changements postnataux normaux tels que la perte de poids, les changements menstruels, la diminution de la libido, ainsi que les changements d'appétit et d'intérêt général [58, 60].

Facteurs de risque. Les facteurs de risque pour la DPN incluent des antécédents médicaux personnels ou familiaux de dépression ou d'autre maladie psychiatrique, le stress psychologique pendant la grossesse et les symptômes dépressifs durant celle-ci. En outre, les facteurs sociaux comme la perception d'isolement social et les problèmes conjugaux au cours de la gestation sont aussi associés avec un risque élevé de la DPN.

Des corrélations modérées ont été observées entre les dépressions prénatale et postnatale [62-65]. Des complications obstétricales incluant la pré-éclampsie, l'hospitalisation pendant la grossesse et l'accouchement par césarienne d'urgence ont en effet été associées à la dépression suivant l'accouchement [64, 66, 67]. Il existe aussi des publications qui suggèrent que le tempérament [68] ou le comportement [69] de l'enfant peuvent être associés avec la DPN, mais il est difficile d'éliminer la possibilité de la causalité inverse pour ces facteurs de risque. Dans certains pays, on avance même qu'une connexion existe entre le sexe de l'enfant et la DPN [70, 71].

Les conséquences de la dépression postnatale. Des liens ont été établis entre la DPN et des retards dans le développement cognitif et linguistique des jeunes enfants [72], ainsi qu'avec des problèmes comportementaux chez ceux-ci [73-75]. Des chercheurs ont également relié la DPN à une

augmentation des visites médicales inattendues pour l'enfant et à un redoublement des coûts des services de santé et des services sociaux, principalement pour les soins de l'enfant, durant la période postnatale immédiate [76].

Les recherches sur les conséquences de la DPN pour l'enfant ont mis l'accent sur l'interaction entre la mère et l'enfant, ainsi que sur les conséquences subséquentes pour son développement. Il a été observé que les mères dépressives ont tendance à faire preuve de moins de sensibilité lors des moments d'interactions. Aussi, les enfants de ces mères ont un risque élevé de développer une relation d'attachement insécurisée [77-79]. Chez les adolescents, des chercheurs ont associé l'histoire de la DPN maternelle à des problèmes de santé mentale incluant la dépression et l'anxiété [80]. Une étude portant sur des effets de la dépression maternelle sur les enfants jusqu'à l'âge de 16 ans a même trouvé une association entre l'histoire de la DPN chez la mère et le quotient intellectuel des adolescents [81]. Il est important de noter que ces effets sont probablement médiés et à d'autres moments confondus par la dépression maternelle.

L'anxiété postnatale. Bien que l'anxiété après l'accouchement puisse avoir des effets néfastes sur l'enfant, celle-ci a tendance à recevoir moins d'attention que la DPN [55]. Le risque d'anxiété postnatale augmente s'il y a eu des problèmes pendant la grossesse ou si l'enfant a un risque élevé de développer des problèmes de santé [55]. Une anxiété postnatale peut nuire à l'interaction mère-enfant. Par ailleurs, la sensibilité ainsi que la capacité de réponse des mères anxieuses envers leur enfant peuvent être aussi compromises, comme c'est le cas avec la dépression maternelle [82]. L'anxiété postnatale est également associée à des problèmes de développement cognitif et de comportement de l'enfant [83].

La psychose postnatale. La psychose postnatale est une urgence psychiatrique qui exige l'hospitalisation et qui est généralement associée avec le trouble bipolaire [84]. La prévalence de la psychose postnatale est entre 1 et 2 pour 1000. Ses caractéristiques incluent la confusion, le délire et

l'hallucination. Cette condition apparaît rapidement pendant les quatre premières semaines suivant l'accouchement et les causes restent incertaines [58, 85, 86].

La naissance prématurée

La naissance prématurée (NP) est définie par l'Organisation mondiale de la Santé comme un accouchement avant 37 semaines complètes de gestation [87], et compte parmi les problèmes actuels les plus importants de l'obstétrique [88-91]. Le taux de la NP au Canada était de 8,2 % des naissances vivantes en 2004 [88]. Les enfants nés prématurément sont à risque de développer de nombreux problèmes de santé, y compris la faiblesse cognitive, la cécité, la surdité et les maladies respiratoires, en plus du risque élevé de décès néonatal [92]. Le taux de prématurité est en augmentation dans plusieurs pays [89, 93, 94], dont le Canada [88], et la capacité de la prédire reste faible [95, 96]. Par conséquent, l'identification des nouveaux facteurs de risques et l'élucidation des associations entre ces derniers et la durée de la gestation sont essentiels afin de définir les stratégies pour en réduire l'incidence, et donc les conséquences de la gestation écourtée.

La prématurité spontanée et induite

L'accouchement prématuré se divise en trois grandes catégories cliniques : la NP provenant d'un travail prématuré, la rupture prématurée des membranes (RPM) et la NP iatrogène (c'est-à-dire un travail prématuré induit ou un accouchement césarien prématuré). Les deux premières catégories sont fréquemment mises ensemble et nommées « la prématurité spontanée ». Le travail prématuré représente environ la moitié des naissances avant terme, alors que la RPM et le NP iatrogène comprennent approximativement le quart des NP chacun [97].

La *late preterm birth* et la *early term birth*

Un nombre croissant de publications suggèrent qu'il y a un taux élevé de morbidité chez les enfants nés vers la fin de cette période de prématurité ou tôt après la 37^{e} semaine de la grossesse. De

plus, ces enfants ont davantage de besoins éducatifs et requièrent plus de soins de santé [98-101]. La naissance à la fin de la période prématurée (*late preterm birth*) est généralement définie comme un accouchement entre 34 et 37 semaines de gestation [102]. Elle compte pour 74 % des naissances prématurées aux États-Unis [103], alors que la naissance précoce mais non prématurée (*early term birth*) est définie comme un accouchement entre 37 et 39 semaines [104] et comprend environ 17,5 % des naissances vivantes [105].

Les facteurs de risque pour l'accouchement prématuré

La prématurité est comprise comme un processus chronique et complexe. On identifie divers facteurs de risque. Plusieurs aspects généraux de la santé et du comportement, dont la dépression, le stress occupationnel, le tabagisme et les déficiences nutritionnelles, sont associés avec la NP [93, 94, 106, 107]. L'histoire reproductive et les complications pendant la grossesse sont également associées à l'âge gestationnel à l'accouchement. Par ailleurs, le taux de prématurité chez les femmes ayant conçu dans un délai de moins de six mois après le dernier accouchement est approximativement le double comparativement aux autres femmes. De leur côté, les gestations multiples sont fortement associées avec la NP : plus de la moitié des grossesses gémellaires et presque 80 % des grossesses d'ordre supérieur (triplés, quadruplés, etc.) se concluent par un accouchement dit prématuré [108, 109]. Un accouchement prématuré antérieur est également un prédicteur important, puisqu'il implique un taux de NP environ 2,5 fois plus élevé [94, 110, 111]. Plus encore, les femmes ayant un historique familial de NP sont plus à risque d'accoucher prématurément [96, 111]. Des maladies médicales, dont l'asthme, le diabète, l'hypertension artérielle et les maladies de la glande thyroïde, sont aussi associées à un risque élevé de NP [94], alors que l'indice de masse corporel avant la grossesse et la prise de poids pendant celle-ci sont associés de façon inverse au risque de NP [88, 97, 106, 112, 113].

Le facteur de risque démographique le plus frappant pour la NP aux États-Unis est le statut minoritaire racial ; le taux d'accouchement prématuré des femmes afro-américaines est à peu près le

double du taux des femmes caucasiennes [94]. Le faible statut socio-économique est un autre facteur de risque clé pour la NP. Des recherches suggèrent que la quantité et la qualité des soins prénataux sont associés de façon inverse avec la NP [114], mais il est probable que ces relations puissent être expliquées en grande partie par des variables socio-économiques [115].

Plusieurs études suggèrent que les femmes aux prises avec du stress psychosocial ou de l'anxiété ont un risque modérément élevé de subir une NP [94, 116-121]. Ces recherches ont utilisées diverses mesures de stress dont les évènements stressants de la vie [117, 122-127], l'anxiété liée à la grossesse [122, 123, 128, 129], le stress perçu [130] et le stress occupationnel [131]. Les chercheurs ont également mis en évidence des liens entre les changements de niveaux de stress pendant la grossesse [132] et les mesures composées du stress [133] avec la NP. Par contre, plusieurs études sur le stress psychosocial et la NP ont eu des résultats négatifs [134-136]. Une présentation plus détaillée de la littérature sur le stress psychosocial pendant la grossesse et la NP sera faite dans le chapitre 3.

Avec la gamme des facteurs de risque discutés ci-dessous, la compréhension de l'interaction entre les diverses variables dans la prédiction de la durée de gestation reste faible. Plusieurs chercheurs ont construit des cadres conceptuels afin de relier et d'organiser des causes et des prédicteurs de la prématurité. La section suivante donne donc un aperçu de tels modèles, tout en mettant l'accent sur le stress psychosocial et l'histoire obstétrique, ces derniers étant parmi les principaux facteurs de risque traités dans cette thèse.

Les cadres conceptuels de la prématurité

St-Laurent et ses collègues ont construit un modèle théorique des déterminants biopsychosociaux de la durée de gestation et de la croissance fœtale [137]. Ce modèle a été développé et testé sur une population de 1602 grossesses uniques dans la région de la Montérégie. Les prédicteurs dominants sont des variables sociodémographiques et psychologiques.

L'équipe de Misra a également développé un modèle qui combine des aspects médicaux et sociaux dans la prédiction de la prématurité [138]. Ce modèle a été construit avec des données provenant d'un échantillon de 739 femmes afro-américaines à faible revenu. Le modèle inclut des variables provenant d'échelles psychologiques comme le stress, le locus de contrôle, la dépression et plusieurs mesures du soutien social, ainsi qu'une composante biomédicale centrée sur l'historique médical général et la grossesse actuelle.

Rauchfuss et Maier ont aussi étudié les prédicteurs biopsychosociaux de l'accouchement prématuré sur une population de 589 femmes dont 29 ont eu une NP [139]. Un antécédent de vaginite était associé avec la NP ($OR > 3.0$, $p < .05$) dans le modèle multivarié final. Par ailleurs, ils ont relevé plusieurs facteurs psychosociaux, notamment certains aspects de la relation conjugale et diverses formes d'anxiété, comme prédicteurs significatifs de la NP.

Hogue et ses collègues [140, 141], ainsi que Dunkel Schetter [118] ont élaboré d'autres cadres conceptuels pour la recherche sur la prématurité. Ces modèles sont axés sur le stress psychosocial et l'anxiété comme facteurs de prédiction, ils seront donc discutés plus en détail au cours des prochains chapitres.

L'Étude de cohorte 3D

Le volet empirique de cette thèse utilise les données provenant de la cohorte 3D, une étude longitudinale qui suit environ 2400 femmes ainsi que leur partenaire et leur enfant, du premier trimestre de la grossesse jusqu'à l'âge de 2 ans de ce dernier. Cette cohorte a été établie pour examiner l'impact de diverses expositions pendant la grossesse sur les issues défavorables de la grossesse et sur les problèmes de santé et de développement de l'enfant. Avec une abondance de données recueillies de façon longitudinale sur un échantillon de trios, l'Étude 3D permettra une amélioration de la

compréhension de la santé périnatale, ainsi que des origines développementales des maladies chroniques.

Objectifs de l'Étude 3D

L'Étude 3D est une ressource disponible pour répondre aux questions concernant les déterminants intra-utérins des issues importantes de la grossesse, dont les anomalies congénitales, la restriction de croissance intra-utérine et la naissance prématurée, ainsi que pour étudier les effets de diverses expositions pendant la grossesse sur le développement au début de l'enfance. En outre, l'étude explore certains effets des technologies de procréation assistée sur la santé de la mère, du fœtus et de l'enfant. L'étude comprend la collecte de données sur les expositions nutritionnelles, environnementales, psychosociales et sur les facteurs socio-économiques, génétiques et épigénétiques.

Population et démarche de l'étude

Recrutement et suivi. L'Étude 3D est axée sur un cadre de trios (mère-partenaire-enfant). La cohorte comprend 2366 femmes recrutées pendant le premier trimestre de la grossesse (8 à 14 semaines) avec un accouchement planifié dans un centre hospitalier participant. Les femmes et leur partenaire sont recrutés à l'un des 10 centres pendant des visites prénatales routinières dans les hôpitaux, ou encore des rencontres d'admission dans des centres de procréation assistée. L'âge des femmes se situe entre 18 et 45 ans au moment du recrutement, et celles-ci parlent couramment le français ou l'anglais. Les critères d'exclusion sont notamment l'usage actuel de drogues illicites, le diagnostic de maladies sévères et les grossesses multiples. Après le recrutement au premier trimestre, les participants sont suivis au deuxième (20 à 24 semaines) et au troisième (32 à 35 semaines) trimestres, ainsi qu'à l'accouchement. Les enfants, eux, sont vus à l'âge de 3 mois, 1 an et 2 ans (Figure 1). Le suivi est effectué par une équipe d'assistants de recherche, d'infirmières et d'autres spécialistes.

Collecte des données et des spécimens biologiques. Les données collectées à l'aide des questionnaires prénataux et postnataux incluent les caractéristiques sociodémographiques maternelles, l'historique médical et les expositions environnementales (Tableau 1). Ces mesures sont également recueillies chez les partenaires participants. Les variables psychosociales comme le stress, l'anxiété et la dépression sont évaluées à l'aide de questionnaires auto-administrés (Tableau 2). Les résultats des échographies de routine sont recueillis, et les expositions nutritionnelles sont calculées avec un journal alimentaire maternel de trois jours, ainsi qu'avec un journal alimentaire de l'enfant à l'âge de 2 ans. L'usage de médicaments sur ordonnance ou en vente libre de même que les suppléments sont enregistrés dans les journaux de médicaments pour la mère et l'enfant. En ce qui concerne les échantillons biologiques, ceux-ci sont prélevés sur les mères, les partenaires et les enfants (Tableau 3). Finalement, le suivi des enfants comprend des évaluations de croissance au cours des 3 visites postnatales, ainsi que les mesures compréhensives des issues neurodéveloppementales à la visite de 2 ans.

Considérations éthiques

Le comité d'éthique de la recherche (CÉR) du centre coordinateur de l'étude, le Centre Hospitalier Universitaire Sainte-Justine, ainsi que les CÉR des centres participants ont tous examiné et approuvé le protocole de recherche, les formulaires de consentement et les affiches de recrutement. Les participants ont le droit de se retirer de l'étude à tout moment, soit de façon partielle (les données et les échantillons biologiques sont conservés), soit de façon complète (toutes les données collectées et tous les échantillons biologiques sont détruits).

Caractérisation de la cohorte

Parmi 8974 femmes approchées pour participer à l'étude, 5669 satisfaisaient les critères et 2456 parmi celles-ci ont accepté de participer, soit 43 % des femmes admissibles (Figure 1). 47 femmes ont subséquemment été jugées inadmissible et 43 se sont retirées de façon complète de l'étude, ce qui

donne un échantillon de 2366 femmes. En raison de considérations éthiques, une comparaison entre les participantes et les non-participantes n'est pas possible. L'âge gestationnel moyen au moment du recrutement est de 11,7 semaines (écarte type, 1,4 semaine). Le taux de données manquantes sur les questionnaires initiaux est faible, avec un maximum de 5,1 % de refus ou de réponse « ne sait pas » pour le revenu familial.

Le Tableau 4 montre les caractéristiques de la population de l'étude à côté de descriptions semblables pour le total des naissances canadiennes [142] et des femmes en âge de se reproduire dans l'Enquête canadienne sur les mesures de la santé (ECMS) [143]. La population de l'Étude 3D est en moyenne plus âgée et de parité moins élevée que les naissances canadiennes en général. L'étude a également un taux plus élevé de mères nées hors du Canada (35 %). La population de notre étude a un niveau de scolarité relativement élevé, avec plus de 60 % des mères ayant suivi une formation universitaire, comparé à 35 % pour le total des naissances canadiennes et 42 % dans l'ECMS. Enfin, les participantes sont plus souvent mariées ou résident avec un partenaire, soit plus que 94 % des mères.

Taux de collecte des données et des échantillons biologiques. Les échantillons biologiques maternels ont été collectés sur une proportion élevée de participants. Les échantillons de sang de 2344 participants ont été recueillis lors d'une visite prénatale (99 %), ainsi que 2352 échantillons d'urine (99 %), 2318 échantillons de sécrétions vaginales (98 %), 1954 échantillons de cheveux (83 %), 1640 échantillons de sang de cordon (74 % des naissances vivantes) et des échantillons placentaires de 1823 participantes (84 %). Les questionnaires auto-administrés, desquels les données psychosociales ont été extraites, ont été remplis par 1811 participantes (77 %) lors de la visite 1, par 1701 participantes (72 %) lors de la visite 2 et par 1573 participantes (66 %) lors de la visite 3. Le suivi postnatal est actuellement en cours, avec 1756 visites de 3 mois déjà terminées, ainsi que 1633 visites d'un an et 1366 visites de deux ans (Figure 1).

Recherches empiriques sur la prématurité dans la cohorte 3D

Cette thèse présente deux études empiriques menées avec les données de la cohorte 3D. Cette dernière est une ressource utile pour l'étude de la prématurité grâce à la vaste collecte de données faite en tenant compte d'une grande gamme de facteurs de risque. L'inclusion de plusieurs mesures psychosociales (par exemple, le stress, l'anxiété et la dépression) à trois moments prénataux constitue une force importante de la cohorte 3D pour explorer diverses questions de recherche sur la santé mentale périnatale. Ainsi, ladite collecte d'informations détaillées sur l'issue et les complications de chaque grossesse antérieure facilite notamment l'étude des séquelles correspondant à plusieurs aspects de l'histoire obstétrique.

Objectifs et plan de la thèse

Cette thèse répond à deux objectifs principaux : (1) la détermination des liens entre des facteurs de risque génétiques et nutritionnels émergents et la dépression postnatale (DPN), et (2) la mesure de l'association entre le stress psychosocial pendant la grossesse (SPG) et la naissance prématurée (NP) au sein de la cohorte 3D. Notre revue de la littérature sur la DPN a révélé que le génotype du transporteur de la sérotonine (SERT) et l'état des acides gras omega-3 polyinsaturés (n-3 PUFA) sont deux facteurs de risque d'intérêt émergeant. Nous avons donc centré notre travail sur ces deux expositions. Le bilan est présenté dans le chapitre 2. À la lumière des considérations méthodologiques, il est devenu évident qu'une étude empirique de ces expositions ne serait pas praticable dans la cohorte 3D à l'heure actuelle. Par conséquent, nous nous sommes concentrés sur le lien entre le SPG et la prématurité.

Nous avons effectué dans le troisième chapitre une revue de la littérature scientifique décrivant les associations et les mécanismes qui relient le stress psychosocial maternel et l'accouchement prématuré. Dans le quatrième chapitre, le deuxième objectif est abordé au cours d'une étude portant sur le rapport existant entre le SPG et la durée de la gestation dans la cohorte 3D. Des analyses plus

poussées sur le stress psychosocial dans la cohorte 3D ont présenté la parité, et plus précisément les résultats des grossesses antérieures, comme des prédicteurs significatifs du stress. Néanmoins, ces dernières n'ont pas été considérées de façon approfondie dans les cadres conceptuels du SPG et de la NP par le passé. Pour pallier cette lacune dans la littérature, nous avons donc examiné de façon formelle les liens établis entre les issues de grossesses antérieures et le stress psychosocial durant la gestation. L'article basé sur cette analyse empirique constitue le chapitre 5. Finalement, le chapitre de conclusion résume les points majeurs de la thèse et suggère quelques directions futures pour la recherche en santé mentale périnatale.

Figure 1. Recrutement et suivi dans l'Étude de cohorte 3D

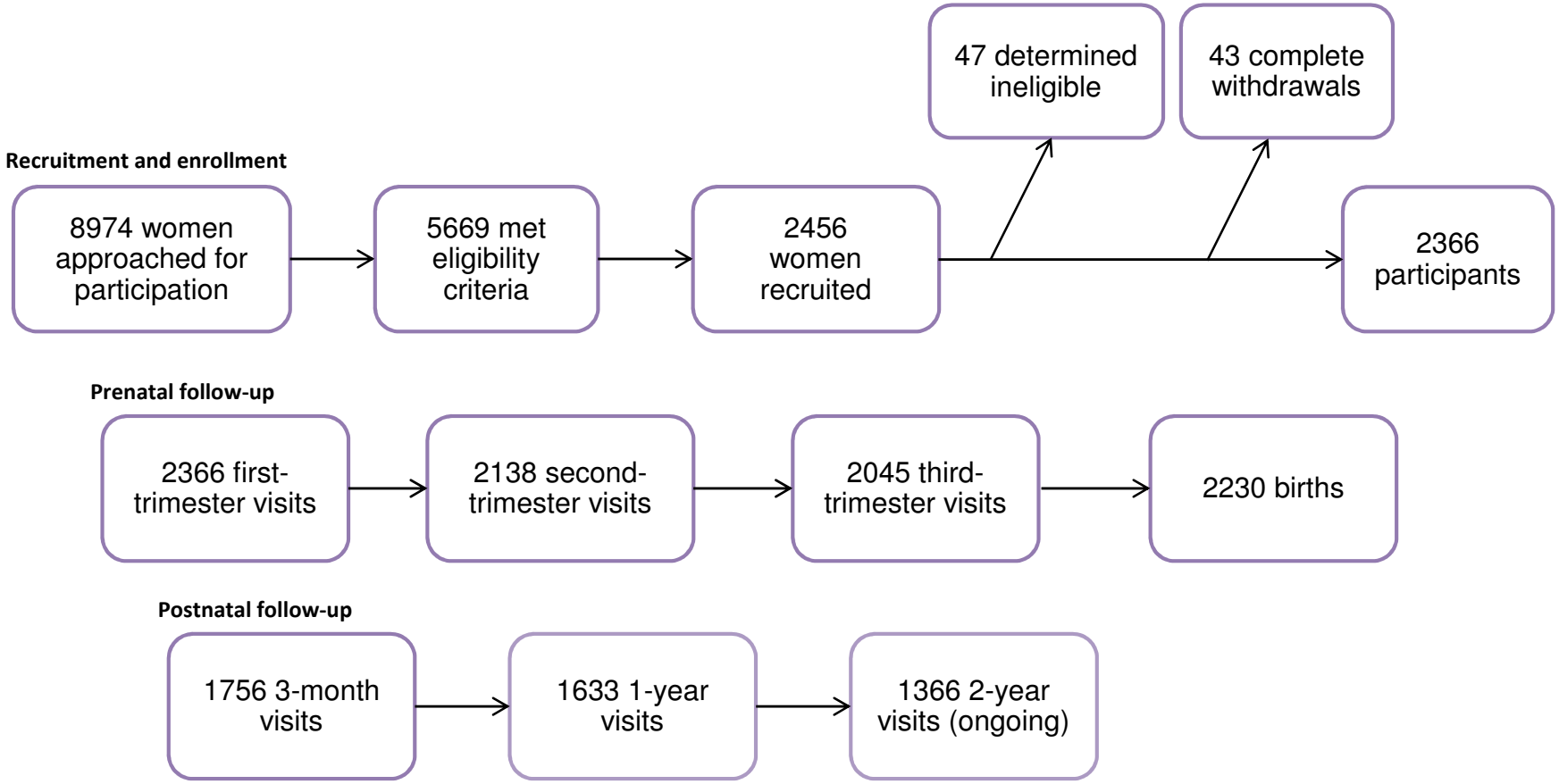

Tableau 1. Mesures démographiques, environnementales et des aspects de la santé maternelle recueillies dans l'Étude de cohorte 3D

	Recruitment (8-14 weeks)	**2nd trimester (20-24 weeks)**	**3rd trimester (32-35 weeks)**	**Delivery / Immediately postpartum**	**3 months postpartum**	**1 year**	**2 years**
Medical history	X						
Vaccination	X	X	X				
Family medical history	X						
Self-reported pregnancy complications	X	X	X				
Infertility, time to pregnancy	X						
Medication, nutrition supplements	X	X	X	X			
Smoking *	X	X	X		X	X	X
Alcohol consumption	X	X	X			X	X
Coffee, tea, energy drinks	X	X	X				
Illicit drug use	X	X	X			X	X
Employment status	X				X	X	X
Neighbourhood and financial support						X	
Self-reported environmental exposures	X		X	X	X		
Sociodemographic characteristics	X				X		X
Anthropometric measurements	X	X	X				
3-day food diary		X					
Ultrasound assessment	Up to 14 weeks	14-28 weeks	28-37 weeks				
Pregnancy chart review				X			

* Les mesures du tabagisme prénatal comprennent l'exposition maternelle à la fumée primaire, secondaire et tertiaire ; les mesures postnatales comprennent l'exposition maternelle à la fumée primaire et secondaire, ainsi que l'exposition de l'enfant à la fumée secondaire.

Tableau 2. Mesures psychosociales maternelles auto-administrées dans l'Étude de cohorte 3D

	Recruitment (8-14 weeks)	**2nd trimester (20-24 weeks)**	**3rd trimester (32-35 weeks)**	**Immediately postpartum**	**3 months**	**1 year**	**2 years**
Physical activity [144]	X	X	X				
Pittsburgh Sleep Quality Index [145]	X	X	X				
Perceived Stress Scale [146]	X	X	X		X	X	X
Pregnancy anxiety measure [147]	X	X	X				
Quality Marriage Index [148]	X	X	X		X	X	X
Marital strain scale [149]					X	X	X
Center for Epidemiologic Studies Depression Scale [50]	X	X	X		X	X	X
Job stress or control scale [150]	X						
Food insecurity	X	X	X	X		X	X
Prenatal Life Events Scale [133]		X					X
Life Orientation Test [151]		X					
Self-esteem scale [152]		X			X		
General Attachment Measure [153]		X					
Anxiety disorders screening instrument		X					
Childhood, adolescence and adulthood					X		

Tableau 3. Spécimens biologiques recueillis dans L'Étude de cohorte 3D

		Recruitment (8-14 weeks)	**2nd Trimester (20-24 weeks)**	**3rd Trimester (32-35 weeks)**	**Delivery / 48 hours postpartum**	**2 years**
Mother	Urine	X	X	X		
	Blood	X	X	X	X	
	Vaginal secretions	X	X			
	Nails			X		
	Hair				X	
Partner	Urine	X				
	Blood	X				
Child	Cord blood				X	
	Umbilical cord				X	
	Placenta samples				X	
	Meconium				X	
	Hair				X	
	Urine					X
	Blood					X

Note : les visites postnatales de 3 mois et de 1 an n'incluent pas la collecte de spécimens biologiques.

Tableau 4. Comparaison des participants de l'Étude de cohorte 3D avec des données sur le total des naissances canadiennes (2010) [142] et avec les participantes du volet biosurveillance de l'Enquête canadienne sur les mesures de la santé (ECMS), cycle 1 (2007-09) [143]

	3D Cohort Study participants (2010-12)	**Canadian births, 2010**	**Canadian Health Measures Survey (2007-09) women 20-39 years of age [a] (95% confidence interval)**
Parity (%): Number of previous viable pregnancies			
0	54.4%	43.3%	49.7% (41.5, 57.9)
1	32.6%	35.3%	16.7% (12.8, 20.6)
2	10.0%	13.8%	25.0% (17.2, 32.7)
3+	3.0%	7.5%	8.6% (5.2, 12.1) [b]
Maternal age (%) (years)			
<20 [c]	0.4%	3.9%	
20–24	7.0%	14.6%	
25–29	31.8%	30.3%	
30–34	38.9%	32.3%	
35+	21.9%	18.9%	
Mean age (years) (SD)	31.0 (4.7)	29.6	29.9 (29.0, 30.8)
Gestational age (weeks)			
Mean (SD)	39.2 (2.2)		
Median	39.6		
Preterm birth (%): <37 weeks	6.2%	7.8%	
Birth weight (g)			
Mean (SD)	3331 (582)	3358	
Median	3370	3386	
Low birth weight (<2500 g) (%)	5.1%	6.2%	
Mother born in Canada (%)	64.9%	72.9%	77.8% (67.6, 88.1)
Infant sex (%)			
Male	50.2%	51.3%	
Female	49.8%	48.7%	

	3D Cohort Study participants (2010-12)	Canadian births, 2010	Canadian Health Measures Survey (2007-09) women 20-39 years of age [a] (95% confidence interval)
Maternal education (%)		[d]	Highest level of education in household
High school or less	9.5%	26.8%	10.7% (4.6, 16.8) [b]
Some college	1.5%		7.9% (3.3, 12.6) [b]
College diploma	26.7%	37.0%	38.9% (30.0, 47.9)
University degree	62.3%	35.1%	42.4% (28.4, 56.5)
Marital status of mother (%)			
Married or common law	94.4%	60.4%	58.7% (51.4, 66.1)
Divorced	0.6%	0.9%	1.4% (0.7, 2.1) [b]
Separated	0.5%	0.4%	2.1% (0.6, 3.5) [b]
Single	4.1%	27.5%	37.8% (30.5, 45.0)
Other/Unknown	0.3%	10.8%	[e]
Fetal death (≥20 weeks) (% of total births)	0.9%	0.7%	
Smoking status (%)		During last 3 months of pregnancy: [d]	
Never	65.2%	89.5% did not smoke	59.9% (52.7, 67.0)
Former	20.0%		19.3% (15.4, 23.1)
Quit during pregnancy			
Current smoker	14.8%	10.5%	20.8% (16.2, 25.5)
Body mass index (kg/m^2)			
Underweight (<18.50)	6.1%		5.3% (2.1, 8.6) [b]
Normal (18.50–24.99)	63.1%		50.4% (39.8, 60.9)
Overweight (25.00–29.99)	18.5%		23.3% (16.2, 30.5)
Obese (>29.99)	12.4%		20.9% (15.6, 26.3)

	3D Cohort Study participants (2010-12)	Canadian births, 2010	Canadian Health Measures Survey (2007-09) women 20-39 years of age [a] (95% confidence interval)
Household income from all sources [f]			
<$20 000	5.6%		10.7% (5.4, 16.0) [b]
$20 000–30 000	5.2%		5.0% (2.7, 7.3) [b]
$30 001–40 000	6.0%		9.0% (4.0, 13.9) [b]
$40 001–50 000	6.0%		9.3% (5.0, 13.6) [b]
$50 001–60 000	6.9%		9.8% (6.6. 13.0)
$60 001–80 000	8.3%		18.2% (14.5, 21.8)
$80 001–100 000	27.7%		9.6% (4.3, 14.9) [b]
>$100 000	29.1%		20.6% (16.1, 25.1)
No response	5.1%		7.8% (3.7, 12.0) [b]

[a] Les estimations sont pondérées pour tenir compte du plan de sondage complexe de l'ECMS.

[b] Grande variabilité de l'échantillonnage. Les données doivent être interprétées avec prudence.

[c] La première catégorie d'âge est définie comme 18 à <20 pour l'Étude de cohorte 3D et comme moins de 20 ans pour les naissances canadiennes.

[d] Source: Référence [154], 2006-2007.

[e] Estimations dont la qualité est inacceptable et qui sont supprimées par Statistique Canada.

[f] Différence de 1 $ dans les catégories de l'Étude de cohorte 3D et Statistique Canada.

Chapter 2

Emerging Risk Factors for Postpartum Depression: Serotonin Transporter Genotype and Omega-3 Fatty Acid Status

Abstract

Objective: Depression is a leading cause of disability and hospitalization. Women are at the highest risk of depression during their childbearing years, and the birth of a child may precipitate a depressive episode in vulnerable women. Postpartum depression (PPD) is associated with diminished maternal somatic health as well as health and developmental problems in their offspring. This review focuses on two PPD risk factors of emerging interest: serotonin transporter (5-HTT) genotype and omega-3 polyunsaturated fatty acid (n-3 PUFA) status.

Method: The MEDLINE, PubMed, and Web of Science databases were searched using the key words postpartum depression, nutrition, omega-3 fatty acids, and serotonin transporter gene. Studies were also located by reviewing the reference lists of selected articles.

Results: Seventy-five articles were identified as relevant to this review. Three carefully conducted studies reported associations between the 5-HTT genotype and PPD. As well, there is accumulating evidence that n-3 PUFA intake is associated with risk of PPD. Preliminary evidence suggests that there could be an interaction between these two emerging risk factors. However, further studies are required to confirm such an interaction and to elucidate the underlying mechanisms.

Conclusions: Evidence to date supports a research agenda clarifying the associations between n-3 PUFAs, the 5-HTT genotype, and PPD. This is of particular interest owing to the high prevalence of poor n-3 PUFA intake among women of childbearing age and the consequent potential for alternative preventive measures and treatments for PPD.

Introduction

Major depressive disorder (MDD) is the most common mental disorder in Canada [1], with a lifetime incidence of 7.9% to 8.6%, a 1-year prevalence of 4% to 5%, and a 6% point prevalence of symptoms consistent with depression [2]. The rate of outpatient treatment for depression increased more than 3-fold in the United States between 1987 and 1997 [3]. Among women of childbearing age, depression is the second-leading cause of disability worldwide [4]. Taken together, depression and other affective disorders constitute the leading cause of nonobstetric hospitalization among women of childbearing age in the United States [5]. In Canada, the incidence and rate of hospitalization for MDD is about 50% higher for women than for men [2, 6]. Finally, it is during the first postpartum year that women are at the highest risk of depression, with 45% to 65% of ever-depressed women having their first episode [7].

Postpartum Depression

Postpartum depression (PPD) is defined as a nonpsychotic depressive illness of mild-to-moderate severity occurring in a mother during the first postnatal year. Though clinically heterogeneous, PPD is distinct from the less severe postpartum blues or baby blues (a mild depressive reaction within the first few days following birth, occurring in 15% to 84% of mothers depending on timing, number of assessments, and criteria used to establish a case) [8] and the much less frequent, though more serious, postpartum psychosis (a psychiatric emergency occurring in fewer than 1 of 500 mothers, with rapid onset within the first 4 weeks after delivery, generally associated with bipolar disorder and requiring hospitalization) [9]. The prevalence of PPD is generally reported as between 10% and 15% [7, 10].

Consequences of PPD

PPD is associated with reduced maternal functional status [11], chronic disease [12] and diminished physical health-related quality of life [13]. PPD has also been linked with numerous somatic and psychiatric problems in the children of depressed mothers [14, 15]. Research suggests that mothers suffering from PPD tend to be more disengaged, hostile, critical, and less sensitive and responsive toward their children [16, 18]. These patterns can lead children to develop an insecure attachment relationship with their mother, resulting in disruptions in sleep patterns, delays in language and cognitive development, poor affect regulation, and other emotional and behavioural problems [19]. For example, 10-year-old children exposed to maternal PPD symptoms since birth have larger left and right amygdala and a heightened cortisol response to stress [20], and other long-term associations have also been observed between maternal PPD and cognitive outcomes including IQ in adolescents [21].

PPD compared with other depression

While the diagnostic criteria for PPD are otherwise identical to those for depression occurring at other times, certain biologic markers distinguish PPD from other types of depression. It is likely that hormonal changes associated with parturition contribute to mood alterations in vulnerable women [22]. Studies have shown decreased susceptibility to depression in women during times of reproductive hormone stability, suggesting that PPD may stem in part from marked hormonal variations associated with childbirth [23]. Over the course of pregnancy, cortisol levels double [24], while progesterone and estradiol levels increase 10 and 50 times respectively; these hormones then abruptly return to normal levels within the first two weeks of the postpartum period [25]. Experimental evidence suggests that women who develop PPD may be particularly sensitive to these hormonal fluctuations [26-28]. Further, decreased levels of monoamines including serotonin (5-HT), norepinephrine, and dopamine are implicated in the pathogenesis of depression [29], and data from animal models suggest that estrogen and other steroid hormones mediate the transcription of genes regulating synthesis and metabolism of

neurotransmitters and their receptors [30, 31], supporting the hypothesis that hormonal fluctuations affect the risk of PPD in part through their effects on the central nervous system. Finally, the prenatal and postpartum periods involve exceptional social stressors and demands on women that have been found to increase both the risk and the consequences of depression [32, 33].

Treatment of PPD

The care and treatment of women with PPD varies widely between countries, owing in part to inadequate guidelines and disparities in accessible treatment options [34]. Nonetheless, there is evidence supporting pharmacologic and other biological interventions (for example, hormonal interventions or bright light therapy) for the treatment of moderate-to-severe depression in postpartum women [35, 36]. While few placebo-controlled trials of antidepressants (ADs) have been conducted in women with PPD, two trials have yielded positive results [37, 38], and ADs appear to be as effective for PPD as for MDD occurring at other times in the life cycle [36]. However, concerns have been raised regarding the robustness of evidence on which these conclusions are based [35], and few studies have compared different classes of medications for the treatment of PPD [39]. In addition, evidence suggests that adherence to ADs during the postpartum period may be poor [34]. Psychotherapeutic and other nonpharmacologic interventions, including relaxation and massage therapy, infant sleep interventions, and maternal exercise, have also shown promise in the treatment of PPD. However, the evidence base concerning their effectiveness is still limited [40, 41].

Risk factors for PPD

Given the limited knowledge regarding efficient and safe treatment of PPD, one avenue for reducing PPD and need for treatment would be through preventive approaches targeting risk factors. A constellation of risk factors for PPD has been identified that includes social, demographic, obstetric, biological, hormonal, psychiatric, and genetic features, as well as characteristics of the newborn child. Among the key social factors predicting PPD are a strained marital relationship, low social support, and

stressful life events [7, 14]. Low socioeconomic status (SES) [42, 43] and personal or family history of depression or mood disorders [14] have also been identified as significant risk factors for PPD. PPD has been linked with severe obstetrical complications during pregnancy [44, 45] and at delivery [46]; with adverse birth outcomes (low birth weight and preterm birth) [47]; and with adverse neonatal outcomes, such as infant irritability and poor motor function [48].

It has also been proposed that the environmental risk for depression may be moderated by genetic factors. It is estimated that about 40% to 50% of the risk for depression is genetic [49], with family studies showing a 3- to 4-fold increased risk of depression for family members with depression, depending on the degree of relation [50]. However, the specific mechanisms of genetic causality are not well understood [25], and the relative contribution of various combinations of genetic and environmental factors to PPD is as yet undetermined.

Beyond social influences, one key environmental factor may be nutrition. There is indeed evidence that diet quality, dietary intake, and overall nutritional status can affect the risk of PPD [51]. Pregnancy is a period during which nutritional requirements and vulnerability to poor nutritional status are heightened. In fact, requirements for many nutrients in women reach a lifetime peak during pregnancy or lactation. Improved nutritional status during these periods may positively impact on maternal mental health, both directly and by augmenting the effectiveness of ADs [51].

Therefore, our review will focus on two risk factors of emerging interest, serotonin transporter (5-HTT) genotype and omega-3 polyunsaturated fatty acid (n-3 PUFA) status. The 5-HTT gene was selected because it has become the most investigated genetic variant in psychiatry, psychology, and neuroscience [52]. Further, a significant body of research has explored the association between n-3 PUFAs and PPD [53-56]. Because n-3 PUFAs are hypothesized to reduce the risk of depression, in part through the regulation of gene expression [53], studies testing the interaction between n-3 PUFAs and genetic exposures in the prediction of PPD would be warranted. This is particularly important as

nutrition is a potentially modifiable environmental risk factor [51, 57] that could interact with a genetic predisposition to PDD.

Literature Search

We searched the MEDLINE (1950 to 2011), PubMed (1966 to 2011), and Web of Science (1965 to 2011) databases for articles in English or French using the key words postpartum depression, nutrition, omega-3 fatty acids, and serotonin transporter gene. We included narrative and systematic reviews, original research reports of observational or experimental studies, and editorials. Studies were also located by reviewing the reference lists of selected articles. Our search generated 257 articles. Abstracts from research reports and systematic reviews were assessed for exposure and outcome measures. To be included, studies needed to have PPD or depressive symptoms as an outcome. At least one of the following exposures was also required: 5-HTT genotype, n-3 PUFA dietary intake, supplementation, or biomarker measurement, and fish consumption. Review articles and editorials addressing these exposures, as well as other genetic and nutritional risk factors for PPD, were included. This left 75 articles forming the core of our narrative review.

The 5-HTT Gene and PPD

Following reports of associations between the short allele of the serotonin transporter gene linked polymorphic region (5-HTTLPR) and anxiety-related personality traits [58], studies have addressed the influence of the 5-HTT gene on depression, both alone [59] and in interaction with environmental risk factors [60]. The 5-HTT gene modulates the reuptake of 5-HT at brain synapses, a principal neurobiological feature of depression and the target of selective serotonin reuptake inhibitor ADs [60].

Nevertheless, the precise relation between 5-HTT and the risk of depression is somewhat controversial, with a recent meta-analysis concluding no overall effect [61]. However, this finding has

been critiqued on several grounds, including heterogeneity in measurement of outcome and environmental exposure, exclusion of studies with high-quality designs [62], inadequate measurement of relevant environmental exposures [62, 63], and use of inappropriate interaction models [64, 65]. Another meta-analysis concluding that positive results for interactions between 5-HTTLPR and stressful life events in the prediction of depression were compatible with chance findings [66] has also been critiqued on some of these same grounds [67]. A third meta-analysis with broader inclusion criteria [68] concluded that 5-HTTLPR moderates the relation between stress and depression. In addition, significant associations between 5-HTTLPR genotype and depression were found in two other meta-analyses that did not take into account stress as a covariable [69, 70]. Accordingly, there are reasons to suspect that the 5-HTT gene is related to depression in some subpopulations, including women in the postpartum period.

Biologic evidence suggests a role of the 5-HT system in PPD that may differ from that in other forms of depression [71]. Synthesis of cerebral 5-HT decreases during pregnancy owing to placental catabolism of tryptophan, the precursor to 5-HT [72]. PPD symptoms are positively correlated with postnatal tryptophan catabolism [73] and inversely correlated with maternal plasma tryptophan concentrations [71]. This suggests that the 5-HT system may be of particular importance in the pathophysiology of depression in postpartum women.

Epidemiologic evidence suggests that 5-HTT gene expression patterns may have differential effects for men and women, particularly in the context of psychosocial stress. One study [74] on 5-HTT, family environmental risk, and depression showed effects for women but not men. Two additional studies [75, 76] showed increased depressive symptoms in females carrying the short allele but a protective effect of the short allele in males.

The 5-HTT genotype was linked to PPD in three other studies. A study [77] looking at depressive symptoms at 3 time points after delivery found a significant positive association between depressive

symptoms and 5-HTT expression level at 8 weeks into the postpartum period. Another study [78] of women with a prior history of depression found that short allele carrier status (either one or two copies of the short allele) of the 5-HTT gene predicted depression at 1- to 8-weeks during the postpartum period (OR 5.13; 95% CI 1.16 to 22.7, p = 0.02). Finally, a recent study [79] showed the 5-HTT short allele to be associated with increased risk of PPD in low-SES women but with decreased risk in high-SES women. Taken together, these heterogeneous results suggest that null findings from other studies [80, 81], particularly meta-analyses [61, 66], may mask interactions between 5-HTT genotype and environmental risk factors.

n-3 PUFA and PPD

Found in fish as well as some seeds and nuts [82], n-3 PUFAs are essential unsaturated fatty acids, and they merit attention and further study for several reasons. First, n-3 PUFAs directly affect brain activities, including receptor function, neurotransmitter uptake, and signal transmission [51], and evidence suggests a beneficial role of n-3 PUFAs in the treatment of patients with diagnosed depression [83, 84]. Second, dietary intake of n-3 PUFAs is particularly poor, and the ratio of n-6 to n-3 PUFA intake has risen dramatically over the last century [85]. This ratio is a commonly used marker of dietary fatty acid composition and is positively related to risk for various diseases [86]. Finally, as n-3 PUFA stores are transferred from the mother to the developing fetus during gestation and later to the infant by lactating mothers, maternal n-3 PUFA levels decrease during pregnancy and remain lowered at least 6 weeks into the postpartum period [87].

Research on n-3 PUFAs and PPD has been informed by an interest in the interrelations between fatty acids, depression, and cardiovascular disease [88, 89]. Patients with depression show increased cardiovascular mortality, and depression is a frequent comorbidity in patients with coronary artery disease and is associated with worse outcomes in these patients [89-91]. Depression and cardiovascular

disease may exacerbate each other directly, but it is also hypothesized that these two seemingly disparate health problems share common causes [92]. n-3 PUFAs are understood to modulate both serotonergic neurotransmission and thrombotic and inflammatory mechanisms associated with coronary disease [90, 93], and it is likely that inflammatory markers comprise part of the physiological mechanism of depression as well [94-97].

Evidence linking n-3 PUFAs and depression spans multiple study designs and populations [85, 98, 99]. Associations have been found in case-control, cross-sectional, and cohort studies; with exposures including blood lipid samples, adipose tissue samples (reflecting long-term or habitual intake), fish consumption, overall dietary fatty acid intake [100], and postmortem brain cortex analyses [101]; and with outcomes including clinical depression, depressive symptoms [99], depression during pregnancy, and PPD [102]. Serum levels of docosahexaenoic acid (DHA), one of the principal n-3 PUFAs associated with depression, have been observed to decline during pregnancy and after delivery, leaving postpartum women vulnerable to DHA deficiency [55, 103]. Dietary intake and serum levels of n-3 PUFAs have been inversely associated with PPD [53, 55] and with depression in other populations [99, 104]. Ecologic and cross-sectional studies [85] have found inverse associations between consumption of fish (a primary dietary source of n-3 PUFAs) and major depression and PPD.

Evaluating research on n-3 PUFAs and PPD must be done with caution. This research is conducted against a background of robust links between psychosocial exposures and affective disorders and strong demonstrated associations between depression, before or during pregnancy, and PPD. An emerging body of research also shows links between depression and other nutrients whose intake is likely to exhibit some collinearity with n-3 PUFAs. Nevertheless, randomized controlled trials have shown n-3 PUFAs to be effective as AD treatment [84, 105], suggesting a causal role for this nutrient class in the etiology of depression. This claim is supported by evidence linking n-3 PUFAs with efficient neurotransmission [106] and with inflammatory mechanisms connected to depression. Several clinical

trials of n-3 PUFA supplementation for patients with MDD have shown large effect sizes [107]. However, meta-analyses suggest it is more realistic to expect moderate effect sizes from supplementation [83, 84]. Observational studies of n-3 PUFAs and depression have also shown moderate effect sizes. For example, in a study [91] of patients with recent acute coronary syndromes (representing a high-risk group), the per cent of phospholipid fatty acids represented by n-3 PUFAs was about 12% lower in people with depression, and the percentage of DHA about 14% lower, compared with nondepressed people.

Finally, it needs to be considered that plasma levels of fatty acids are an imperfect measure of dietary intake and also an imperfect predictor of fatty acid levels in brain tissue. Serum fatty acid levels have been shown to be sensitive to recent changes in dietary fatty acid intake in adults [108-110]. This pattern has specifically been observed in pregnant women, with n-3 PUFA supplementation associated with elevated plasma and postpartum breast milk DHA levels [111]. Findings from animal studies [85, 112] suggest a robust relation between serum and brain fatty acid levels, and dietary deficiency in n-3 PUFAs has been associated with observed changes in brain composition and neural functioning in animal models [85]. Significantly, n-3 PUFA deficiency has been associated with altered metabolism of dopamine and 5-HT [109], two of the key neurotransmitters underlying the neural physiology of depression. However, animal models show the mechanisms through which fatty acids are absorbed, converted, synthesized, and processed in the brain are complex and change over the life course [109, 113-118]. Dietary fatty acid intake affects brain fatty acid levels most readily during early development [119-121], and it is unclear how quickly brain fatty acid levels change in relation to dietary intake in mature animals. Nevertheless, significant changes in brain fatty acid levels were observed in adult female rats within a time span of one reproductive cycle following diet modification [122].

n-3 PUFA status and modification of intake

Evidence from numerous fronts suggests that intakes of n-3 PUFAs are far below recommended levels and are amenable to improvement. In the US adult population, intake of DHA and eicosapentaenoic acid (EPA) in 2000 was more than 70% below recommendations from the National Institutes of Health [123]. A 4-fold increase in fish consumption would be required to bring EPA and DHA intake to recommended levels. In Canada and Australia, maternal milk concentrations of DHA appear to have decreased by about 50% over the 15-year period ending in 1999 [124].

Inadequate n-3 PUFA levels are of even greater concern in pregnant women. In a cross-sectional survey [125] of pregnant women in central Mexico, the median DHA and EPA intakes, as calculated from a food frequency questionnaire, were 55 and 18 mg/day, respectively. This compares with recommendations by the American Dietetic Association and Dietitians of Canada of 500 mg/day DHA and EPA combined [126]. A Canadian study [127] of adults in Québec found that 85% had an EPA and DHA intake lower than this recommendation. Among the women of childbearing age in that study, median intake of DHA was 126 mg/day [127], while a study [124] of pregnant women in British Columbia showed a mean DHA intake of 160 mg/day.

Because maternal plasma n-3 PUFA concentrations decline substantially after delivery [128, 129], maintaining a sufficient intake of n-3 PUFAs is important to ensure adequate fatty acid stores during the postpartum period. In addition to the implications for maternal mental health, n-3 PUFAs are essential for infant neural and visual development [130]. n-3 PUFA intake is thus critical for lactating mothers. While there has been considerable focus on n-3 PUFA status in adolescent mothers owing to the enhanced nutritional risks associated with adolescence [131], several studies have also examined n-3 PUFA levels in adult postpartum women. Two studies found DHA intake of 30 to 58 mg/day and concentration in breast milk of about 0.10%, well below recommendations of 0.2% to 0.4% [132, 133]. A study comparing lactating and nonlactating women found a DHA intake of 29 to 47 mg/day and EPA

intake of 52 to 91 mg/day [128], again well below recommendations. These results suggest poor maternal n-3 PUFA intake to be a significant problem, not only during pregnancy but also in the postpartum period.

n-3 PUFA, 5-HTT Genotype, and PPD

A growing body of literature is exploring nutritional aspects of depression [134] and PPD specifically [25, 51]. However, little research has addressed interactions between nutritional and genetic risk factors in the prediction and etiology of depression. There has been considerable focus on interactions between the 5-HTT gene and psychosocial stress [68, 135] but little investigation into genetic interactions with nutritional exposures that may exhibit some of the same effects as stress on brain function. Two studies examining the seasonal variation in n-3 PUFAs, plasma tryptophan, and serotonergic markers [136, 137] suggest that fatty acid levels in the brain may modulate 5-HT release and reuptake. These findings support research into interactions between n-3 PUFAs and the 5-HTT gene and suggest that these two seemingly disparate exposures may affect the risk of PPD through a common neurobiological mechanism. Accordingly, studying their association in the prediction of PPD may help further elucidate the neurobiological underpinnings of this condition while helping to target prevention and treatment efforts.

Conclusion

There is a growing awareness of the importance of nutritional and genetic exposures as risk factors for PPD. The 5-HTT gene is a promising avenue for genetic research, and it appears highly likely that this gene affects the risk of depression and other psychiatric conditions. However, it is unclear which genotypes are associated with elevated risk in which populations, and specifically how associations between 5-HTT genotype and depression may differ during the perinatal period from other

time points across the life course. Similarly, increasing evidence links n-3 PUFAs with depression in diverse populations. However, the biological mechanisms through which these links function, and the ways in which they may be modified in pregnancy, are not clearly understood.

One of these mechanisms could operate through a gene-environment interaction. Because it can be reasonably hypothesized that the 5-HTT genotype and n-3 PUFAs impact on the risk of PPD, in part through the same mechanism, studying them jointly would present an opportunity to advance our understanding of how genetic and dietary exposures may interact in the etiology of PPD. Knowledge garnered from this effort has the potential to improve the prediction, prevention, and treatment of this significant public health problem. This is particularly important as current intake of n-3 PUFAs in pregnant women is well below recommendations and amenable to improvement.

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Information sur l'article

Chapitre 2 : Emerging Risk Factors for Postpartum Depression: Serotonin Transporter Genotype and Omega-3 Fatty Acid Status

Titre de l'article : Emerging Risk Factors for Postpartum Depression: Serotonin Transporter Genotype and Omega-3 Fatty Acid Status

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Depuis la publication de la revue de littérature qui constitue le second chapitre de la thèse, plusieurs études corroborent les résultats déjà trouvés sur la relation entre les n-3 PUFA et la DPN. Par exemple, une petite étude de cohorte portant sur 43 femmes en Norvège a examiné le rapport entre les taux sanguins de plusieurs acides gras au troisième trimestre de la grossesse et les symptômes dépressifs 3 mois après l'accouchement. Les chercheurs ont trouvé des associations statistiquement significatives entre le DHA, le DPA, le ratio n-3/n-6 et les scores sur une échelle des symptômes dépressifs [155]. Aux États-Unis, une recommandation conjointe de la FDA et de l'EPA a souligné l'importance de la consommation de ces acides gras, tout en clarifiant les quantités recommandées pour différents types de poisson selon leur niveau de méthylmercure [156].

Malgré ces résultats importants, d'autres résultats négatifs ont également été observés. Une étude sur 911 femmes a décelé de faibles différences entre les niveaux des n-3 PUFA liées à la DPN, et ce, selon une des deux échelles de dépistage utilisées seulement [157]. Une autre analyse sur une cohorte de plus de 14 000 mères n'a pas trouvé de lien robuste entre les n-3 PUFA (DHA et EPA) et la DPN [158]. Malgré des observations expérimentales chez les modèles animaux concernant l'efficacité de la supplémentation des n-3 PUFA [159], celle-ci n'a pas été démontrée de façon consistante auprès des populations humaines. Un essai randomisé contrôlé comprenant 126 femmes n'a par ailleurs pas établi de différence, quant aux symptômes dépressifs ou au diagnostic de dépression majeure, entre les groupes de supplémentation des n-3 PUFAs (EPA et DHA) et le groupe placébo [160]. Des revues de littérature scientifique récentes ont constaté que la documentation actuelle ne soutient pas la supplémentation pour la prévention [161-163], ni pour le traitement de la DPN [163].

Divers projets de recherche continuent d'explorer l'influence du génotype 5-HTT sur la dépression. L'importance de la sérotonine dans le cadre de la dépression est soutenue par une méta-analyse de 18 études d'imagerie moléculaire qui a trouvé des réductions de sérotonine dans le mésencéphale et les amygdales des sujets dépressifs [164]. Plusieurs études épidémiologiques ont

également démontré les effets du génotype 5-HTT sur la dépression, soit comme facteur de risque individuel [165], soit en interaction avec d'autres facteurs de risque, comme des évènements stressants [166], la séparation d'un proche [167] et la maltraitance pendant l'enfance [168].

Deux études récentes viennent renforcer l'importance du génotype 5-HTT comme facteur de risque de la dépression périnatale. La première est une étude chinoise de 220 femmes ayant eu un diagnostic de dépression majeure dans la première année suivant la naissance d'un enfant ainsi que de 192 sujets témoins. Cette étude a examiné les variantes du génotype 5-HTT et le stress environnemental. Les investigateurs ont fait valoir que chez les femmes portant l'allèle long du génotype 5-HTT, il y avait un risque élevé de développer des symptômes dépressifs associés aux évènements stressants de la vie, ainsi qu'aux infections ou complications pendant la grossesse [169]. La seconde étude, portant sur une cohorte de 276 femmes brésiliennes, a également trouvé une interaction entre l'allèle long du génotype 5-HTT et les évènements stressants de la vie pendant la grossesse pour la prédiction des symptômes dépressifs 2 à 3 mois après l'accouchement [170].

Afin de poursuivre notre questionnement sur la santé mentale périnatale des mères, nous nous tournons maintenant vers la deuxième question de recherche principale de la thèse, à savoir la relation entre le stress psychosocial pendant la grossesse (SPG) et la naissance prématurée (NP). Avant d'examiner cette question de façon empirique, nous effectuerons d'abord une revue de la littérature sur ce sujet, avec une évaluation des connaissances publiées sur cette association ainsi qu'une discussion des mécanismes biologiques établis et hypothétiques liant le SPG et la NP.

Chapter 3

Psychosocial Stress in Pregnancy and Preterm Birth: Associations and Mechanisms

Abstract

Aims: Psychosocial stress during pregnancy (PSP) is a risk factor of growing interest in the etiology of preterm birth (PTB). This literature review assesses the published evidence concerning the association between PSP and PTB, highlighting established and hypothesized physiological pathways mediating this association.

Method: The PubMed and Web of Science databases were searched using the keywords "psychosocial stress", "pregnancy", "pregnancy stress", "preterm", "preterm birth", "gestational age", "anxiety", and "social support". After applying the exclusion criteria, the search produced 107 articles.

Results: The association of PSP with PTB varied according to the dimensions and timing of PSP. Stronger associations were generally found in early pregnancy, and most studies demonstrating positive results found moderate effect sizes, with risk ratios between 1.2 and 2.1. Subjective perception of stress and pregnancy-related anxiety appeared to be the stress measures most closely associated with PTB. Potential physiological pathways identified included behavioral, infectious, neuroinflammatory, and neuroendocrine mechanisms.

Conclusions: Future research should examine the biological pathways of these different psychosocial stress dimensions and at multiple time points across pregnancy. Culture-independent characterization of the vaginal microbiome and noninvasive monitoring of cholinergic activity represent two exciting frontiers in this research.

Introduction

Preterm birth (PTB) is a significant and growing public health problem leading to increased neonatal morbidity and mortality and entailing substantial social and economic costs [1]. PTB is the leading cause of infant mortality in industrialized countries, accounting for 60% of perinatal mortality and about half of long-term neurological morbidity [2]. There is also mounting evidence linking PTB to health outcomes in adulthood [3]. Despite the identification of numerous determinants of PTB, only about half of preterm deliveries are preceded by a known risk factor [4]. Thus, prediction of PTB remains poor. Identification of novel risk factors and elucidation of the pathways linking risk factors to PTB are therefore crucial research priorities.

PTB is defined as delivery before 37 completed weeks of gestation. In 2004, the rate of PTB was 12.5% of live births in the USA [5] and 8.2% in Canada [6]. Disturbingly, PTB rates are increasing in many industrialized countries [7] and exhibit significant disparities across racial groups and socioeconomic strata [5, 8]. Preterm labour accounts for about half of all PTBs, whereas preterm premature rupture of membranes and iatrogenic causes each account for roughly a quarter. Preterm infants are at increased risk of respiratory distress, jaundice, hypoglycemia, and neonatal death, as well as developmental delays and needs for special education [9]. Annual costs for preterm infants in the USA are estimated at more than $26 billion. PTB also exacts an emotional and financial burden on parents, increasing maternal distress and depressive symptoms [5].

PTB is currently understood to be a complex process stemming from multiple risk factors including genetics, health behaviours, reproductive history, mental health problems, and medical disorders [4, 10]. A growing literature supports the role of psychosocial stress during pregnancy (PSP) in the etiology of PTB [11, 12]. PSP and PTB are connected through neuroendocrine, inflammatory, and maternal lifestyle and behavioral pathways [13-15]. However, there is as yet no consensus concerning (a) which measures of PSP are most strongly associated with PTB, (b) whether there are critical time

windows for the effects of PSP on PTB, (c) the cumulative effects of chronic stress, and (d) the roles played by different pathways in mediating associations between maternal stress and birth outcomes. This selective review of the literature will address these knowledge gaps by assessing the published evidence on the association between PSP and PTB and will highlight established and hypothesized physiological pathways mediating this relationship.

Method

We searched the PubMed and Web of Science databases using the keywords "psychosocial stress", "pregnancy", "pregnancy stress", "preterm", "preterm birth", "gestational age", "anxiety", and "social support". Our original search returned 352 articles. To be considered for inclusion, studies needed to be presented in English and to have PTB or gestational age as an outcome. At least one of the following exposures was also required: stressful life events, perceived stress, anxiety, and social support. We considered original research reports of observational studies as well as narrative and systematic reviews. Relevant studies were also located by reviewing the reference list of selected articles. This left 107 articles from which we constructed the core of our literature review. In light of space limitations and because our goal was to construct a selective review illustrating key current issues in this literature rather than a comprehensive systematic and quantitative review, we do not reference findings from all articles in our literature search. However, we do provide a complete list of core references in Appendix 1.

PSP and PTB

Several indicators of PSP including stressful life events, perceived stress, and pregnancy-related anxiety have been associated with PTB [15-18]. There is some understanding of the biological pathways underlying these links and how they vary across pregnancy, but it remains incomplete. Although results

vary by dimensions targeted and timing of exposure, most studies demonstrating positive results have found moderate effect sizes, with risk ratios between 1.2 and 2.1 for the highest stress scores compared with the lowest across a heterogeneous range of stress measurement scales. The following sections summarize existing knowledge on the measurement of PSP and on its association with PTB.

Measures of PSP

Stress constitutes a psychophysiological consequence of any event challenging an individual's capacity to cope. Stressful life events are situations likely to require some degree of coping in ongoing life adjustment, whereas perceived stress is defined as the degree to which situations in one's life are appraised as stressful. Anxiety is a related subjective concept measuring individual psychological and physical manifestation of exposure to perceived stress. Anxiety is traditionally separated into state anxiety (an emotional response to stimuli perceived as dangerous, threatening, or stressful, typically experienced as tension, worry, or nervousness – or how one feels at a given moment, for example, because of an upcoming interview or test) and trait anxiety (the predisposition to react to a wider range of stimuli by experiencing anxiety – or how one feels generally) [19]. In this review, we examine self-reported subclinical measures of anxiety during pregnancy. Clinical anxiety disorders such as generalized anxiety disorder, panic disorder, and obsessive-compulsive disorder and their comorbidity with major depressive disorder are also likely to impact on obstetric and neonatal outcomes [20], and addressing links between clinical disorders and PTB can further be complicated by the effects of psychotropic medication [21] and other forms of self-medication such as substance use. Consequently, the study of clinical anxiety in the prediction of PTB adds a level of complexity that falls outside the scope of this review.

Research on PSP has examined the roles of both objective stress constructs (i.e., exposures measured independently of the individual's perception of them such as a death in the family, becoming unemployed, natural disasters, or war-related violence) and subjective measures of stress levels. Not

surprisingly, these two concepts are moderately correlated with each other [22]. Studies have also explored the role of "pregnancy-related stress", i.e., stress and anxiety stemming from the pregnancy. Measures of pregnancy-related anxiety capture this concept by asking about fears and concerns specifically related to the pregnancy [23]. Other examples of pregnancy-related stressors include physical changes naturally associated with pregnancy, concerns about the experience of childbirth and parenting, and relationship strains due to pregnancy [24]. Examining the role played by pregnancy- vs. nonpregnancy-related stressors is crucial in understanding how psychosocial stress differs in pregnant women compared with other populations and clarifying what kinds of stressors have the strongest impact on birth outcomes.

Stressful life events, their timing and perceived impact

Stressful life events during pregnancy have been associated with PTB or shortened gestation in some [17, 22, 25-28] but not all [29-32] studies. The studies we reviewed that found effects of stressful life events during pregnancy on PTB were conducted in several different countries, had sample sizes ranging from fewer than 200 to more than 8000, and used both cohort and case-control designs. As the techniques used in measuring stressful life events have been refined, timing within the pregnancy and subjective perception of stress have usually been found to be stronger predictors of PTB than objective event counts across pregnancy [16, 33]. This finding was supported by our review; of the four studies we reviewed on stressful life events that did not find effects, two looked at life events globally across the entire pregnancy and only one measured the perceived impact of life events. In one of the earliest studies of stressful life events and PTB that did find effects, Hedegaard et al. [17] found one or more life events assessed as highly stressful at 30 weeks but not at 16 weeks was associated with a lower gestational age at delivery and increased risk of PTB. No association was found for life events evaluated independently of their subjectively perceived impact. This latter finding helped researchers shift attention from event counts to perception of stressful life events. However, the first finding led authors

to propose that timing of delivery is likely to be determined toward the end of pregnancy, but subsequent biological evidence has not supported this hypothesis. Specifically, the maternal hypothalamic-pituitary-adrenal (HPA) axis has been shown to be progressively downregulated over the course of pregnancy [34], suggesting that biological and emotional stress responses may be attenuated toward the end of pregnancy. In light of this evidence, it is not surprising that life events experienced at the beginning of pregnancy were perceived as more stressful than similar events occurring in the third trimester [35]. A later prospective cohort study supported this view and found that after adjustment for confounders, life events perceived as severely stressful were only associated with PTB when experienced during the first and second trimesters of pregnancy but not the third [26]. Thus, this epidemiological study failed to replicate the finding of Hedegaard et al. regarding exposure to stressful life events later in pregnancy and found instead that earlier exposure was more likely to be associated with PTB.

Studies of pregnant women exposed to traumatic acute events also support this view. In a retrospective cohort study of women who were pregnant during or after a 1998 ice storm in Quebec, Canada, Dancause et al. [36] found a trend toward shorter gestational age at delivery among women in the first or second trimester of pregnancy at the time of the ice storm compared with those who were in the third trimester or became pregnant within 3 months following the storm (when stress hormone levels could still be elevated). In a similar study examining timing in relation to pregnancy of a 1994 California earthquake and length of gestation, earlier exposure was significantly associated with shorter gestation [37]. Other studies assessing the effects of acute exposure to natural disasters, war, and terrorism during pregnancy have also found these stressors to present highest risk early in pregnancy. In sum, observational research supports a stronger role for subjectively perceived stress in the prediction of PTB compared with objectively defined stressful events as well as a stronger role for stressors experienced early compared with later in the pregnancy [16, 33].

General perceived stress and maternal anxiety

An important limitation of the "life event" approach to stress in PTB research is that it often fails to capture relevant chronic stressors such as racism, domestic violence, and less severe "daily hassles". In contrast, the assessment of perceived stress is not necessarily tied to specific events and is thus likely to capture individuals' actual stress levels more precisely than objective scales of stressful life events [16]. Measures of anxiety also share this advantage in that they are not bound to specific events experienced by an individual.

Both anxiety and general perceptions of stress (independent of its source) have been associated with shortened gestation in many [27, 31, 32, 38-43] but not all [29, 44] studies. Our review revealed that studies with null findings tended to be characterized by study populations of higher socioeconomic status and exposure measurement scales not specific to pregnancy. Trait anxiety measures have generally not shown strong direct relationships with birth outcomes, which is likely because they are not sensitive to the presence of stressful stimuli that may trigger state anxiety [45]. Some studies have in fact found protective effects for trait anxiety [46, 47], which may be attributable to a cautious attitude regarding problems or complications arising during the pregnancy. Trait anxiety has, however, shown positive correlations with shortened gestation when combined with more severe risk factors. For example, an inverse correlation between trait anxiety and gestational duration was observed in a study of Swedish women who were in the first trimester of pregnancy at the time of exposure to a clear acute stressor, the Chernobyl nuclear disaster [48].

In contrast to trait anxiety, several studies have found positive associations between pregnancy-related anxiety and PTB or shortened gestation [27, 41, 47, 49]. One prospective cohort study found pregnancy-related anxiety to be associated in a dose-response fashion with increasing adjusted odds of spontaneous PTB [41], whereas another prospective study found an increased risk of PTB among women with high levels of pregnancy-related anxiety and among those who experienced life events with

perceived negative impact [27]. In an attempt to examine both trait anxiety and pregnancy-related anxiety independently, one study found pregnancy-related anxiety was associated with an increased risk of PTB, whereas a protective effect was observed for trait anxiety [47]. Overall, our review suggests that pregnancy-related anxiety may in fact contribute more powerfully to adverse birth outcomes than non-pregnancy-related stressors and that it is a more consistent predictor of PTB than other prenatal stress measures.

Effects of social support

One promising avenue of inquiry in pregnancy research is the possibility that social support may buffer the impact of PSP. Social support is defined by the exchange of social resources between individuals. Although research on the relationship between social support and physical and mental health has been complicated by great heterogeneity of measurement, there is broad consensus on the conceptual division of social support into emotional, informational, and instrumental support [50, 51]. Social support has been hypothesized to affect health through pathways that are relevant to PTB including changes in health behaviors and increased resistance to infection [51].

Social support is conceptually understood to affect health both through direct mechanisms and by buffering the association between stressors and health [41]. Social support has been found to influence perceived stress in pregnant women [52], and it has been hypothesized that social support could mitigate the impact of PSP on PTB. Epidemiological studies have shown inverse correlations between social support and stress biomarkers (e.g., adrenocorticotropin hormone, β-endorphin, cortisol) in pregnant women [53], suggesting that the effects of stress during pregnancy on birth outcomes may be amenable to intervention. However, research examining the relationship between social support during pregnancy and birth outcomes has yielded disappointing results, with numerous null findings in both observational studies and clinical trials looking at PTB [42, 51, 54, 55]. Positive results have been observed in a small number of studies. One case-control study examining paternal

support found a trend toward reduced PTB and buffering of the effect of chronic stress among women with higher levels of partner support [31]. A randomized trial of nurse home visitation found a reduced rate of PTB in two high-risk subgroups of the intervention arm, smokers and young adolescents [56]. Another positive subgroup finding was observed in an intervention trial of paraprofessional home visit support to pregnant teenage women. This study found a reduction in PTB among unmarried mothers in the intervention group [57]. Importantly, mothers in the intervention group were more likely to receive adequate prenatal care than those in the control group, yet the effect of the intervention on PTB persisted after adjustment for adequacy of prenatal care. This suggests that in certain high-risk populations, effective social support interventions can improve birth outcomes both through health care services (likely in response to informational support) and via more direct pathways that may stem from emotional or instrumental support. Overall, in light of the scattered positive findings in this area, further research is needed to clarify the effects of women's existing social support on PTB. That research could address what components would make up the most promising social support interventions and which populations should be targeted.

Combined exposure measures

Different dimensions of PSP are correlated with each other [33, 39, 40, 58], suggesting that the various measures capture overlapping domains. To account for this intersection, some investigators have combined multiple exposure concepts into latent variable constructs. One such study used structural equation modeling techniques to combine state anxiety, perceived general stress, life events, and pregnancy-related stress into a single latent variable. The latent stress factor significantly predicted gestational age at delivery, although pregnancy-related stress was a better predictor than the latent factor [32]. In an earlier cohort study [45], prenatal stress was operationalized using a combination of perceived stress, state anxiety, and life events. This latent variable significantly predicted timing of delivery. In one prospective study examining several measures of anxiety and personal resources [40],

state anxiety and pregnancy-related anxiety were loaded on a single factor labeled “stress” that was found to be significantly correlated with length of gestation and was predictive of PTB. Finally, a study combined perceived stress, state anxiety, and pregnancy-related anxiety, each measured at three time points across pregnancy, using a longitudinal latent trait-state model [39]. In this study, only pregnancy-related anxiety experienced throughout the course of pregnancy was associated with shorter gestation after controlling for known risk factors.

Mechanisms Linking PSP with PTB

Biological mediators of the relationship between PSP and PTB include neuroinflammatory, immune, and neuroendocrine pathways [13, 16, 24]. In addition, stress-related behaviors including smoking, substance abuse, and poor nutritional intake have been implicated in the etiology of PTB [13]. Finally, pregnancy-related anxiety may sometimes stem from medical risk that itself leads to PTB. Figure 1 provides a partial schematic of the key variables connecting PSP to PTB through the pathways discussed below.

Research directly exploring biological and behavioral mechanisms mediating the relationship between PSP and PTB is scarce. Rather, these mechanisms must at present be triangulated from epidemiological studies and research conducted using animal models. The few studies that have attempted to describe connections between psychological stress, biological stress markers, and PTB have generally examined PTB prediction models using both types of stress measures concurrently [59, 60] or have reported inconclusive results when connecting both types of stress measures with birth outcomes [61-63].

Hormonal and neurological correlates of psychosocial stress

The biological manifestations of stress have been assessed from hormone levels in tissue samples as well as through measurement of dopaminergic activity and prefrontal functional connectivity

using positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) scans [64, 65]. For example, experimentally induced mild psychosocial stress has increased dopamine release and dopaminergic activity in the prefrontal cortex (PFC) [64]. Importantly, stress was associated with reduced attention control and functional connectivity in the PFC in a manner persisting beyond the experience of acute stress but that was reversible in response to reduced chronic stress [65].

Psychosocial stress is generally understood to positively correlate with salivary cortisol. Stress is also often directly correlated with corticotropin-releasing hormone (CRH), although negative results have been observed in late pregnancy and inverse correlations were found with chronic stress. Experimental introduction of chronic psychosocial conflict has also been shown to reduce CRH binding sites in the brain of adult tree shrews [66].

Effects of chronic stress

Results from both animal and human studies show associations between psychosocial stressors and alterations in the amygdalic and hippocampal reaction to novel stressors as well as with elevated serum CRH levels and CRH gene expression in the amygdala. This suggests the hypothesis that chronic stress may prime an individual to an adaptive state of hypervigilance and by a process of sensitization increase the physiological responses to future acute stressors [67]. Conversely, chronic stress is also hypothesized to blunt HPA function and has been shown to desensitize the stress response in the entorhinal cortex and striatum of adult rats exposed to chronic prenatal stress [68]. Finally, chronic stress increases susceptibility to infection and is associated with maternal infection during pregnancy. In sum, the relative contribution of chronic vs. acute stress to PTB requires further research.

Neuroinflammatory pathways

Inflammation is the basic process by which tissues of the body respond to injury through the effects of cytokines and other inflammatory mediators. Cytokines are small soluble peptides or glycoproteins including interleukins (ILs), chemokines, and tumor necrosis factor (TNF), among others.

Cytokines' primary function is intercellular communication, and their role in the inflammatory response functions largely through regulation of the immune response [69]. PSP is hypothesized to bring about parturition in part through proinflammatory mechanisms [10], specifically proinflammatory cytokines [70]. As alluded to above, conclusive links connecting psychosocial stress, inflammation, and PTB have not been demonstrated.

However, a considerable body of evidence supports this mediation hypothesis. For example, psychosocial stress leads to increased production of proinflammatory cytokines in the general population [15], and altered levels of inflammatory cytokines have been observed in pregnant women with increased psychosocial stress [14, 15]. Although the specific effects of PSP on the inflammatory response during pregnancy and subsequent birth outcomes have not been precisely described [15], it has been shown that an inflammatory response in the form of overexpression of toll-like receptors in the chorioamniotic membranes is part of normal term labour [71]. Further supporting the role inflammation in parturition, inflammatory cytokines increase the production of prostaglandins, which are implicated in term and preterm labour [72]. Through induction of matrix metalloproteinases, inflammatory cytokines can also weaken fetal membranes and ripen the cervix [73]. A recent meta-analysis found that the inflammatory cytokine IL-6 and C-reactive protein were strongly associated with spontaneous PTB [74], and biological evidence also supports the role of TNF-α in preterm parturition [69]. In addition to the role of the inflammatory response in spontaneous PTB, inflammation has been causally linked with indications for induced preterm delivery (hypertensive disorders of pregnancy). Specifically, features of preeclampsia such as adipocycte lipolysis, de novo hepatic fatty acid oxidation, and impaired prostacyclin and nitric oxide production can be induced by inflammatory cytokines, and the clinical severity of preeclampsia has been associated in a dose-response fashion with cytokine function [15, 75].

Recent work has begun to describe a cholinergic anti-inflammatory pathway (CAP) in which the release of inflammatory cytokines is controlled through the vagus nerve. Specifically, action potentials transmitted through the vagus nerve result in the release of acetylcholine, which inhibits cytokine production by innate immune cells in tissues innervated by the vagus nerve. Evidence in support of this pathway comes from suppression of inflammation (decreased production of proinflammatory cytokines with no change in production of anti-inflammatory cytokines) in response to stimulation of the vagus nerve in adult animal models [76]. Specifically, vagus nerve stimulation inhibits inflammatory cytokine production in an adult rat model of sepsis [77], in a mouse model of pancreatitis [78], and in postoperative ileus [79]. In addition, clinical-pathological studies in adult human subjects with chronic inflammatory conditions show that increased spontaneous CAP activity is correlated to decreased levels of proinflammatory cytokines such as IL-1β.

The relevance of this line of research to the link between PSP and PTB is suggested by results showing a dampening of the connection between inflammation in response to decreased vagal nerve activity and depression (i.e., mouse model studied through monoamine depletion and maternal separation) [80]. This line of work is beginning to map out connections between the brain and inflammatory response that could provide a crucial link connecting neural responses to stress during pregnancy with inflammation-mediated adverse birth outcomes. Of note, CAP activity can be monitored non-invasively via heart rate variability (HRV) derived from maternal or fetal electrocardiogram (ECG). This opens a new, very cost-effective venue for exploring the relationships among PSP, maternal and fetal CAP, inflammation, and PTB in prospective clinical studies.

Infectious pathways and maternal microbiome

Infection is a well-documented risk factor for PTB and is likely to partially mediate the relationship between PSP and PTB. Bacterial vaginosis, the most common lower genital tract infection in women of reproductive age, is associated with stress in pregnant women and with a 1.5- to 3-fold

increase in risk for preterm labour. However, the current characterization of intrauterine infection is imprecise. Numerous different bacteria are known to comprise the vaginal flora, yet clinical tests for infection rely on measures that are relatively crude and sometimes inconsistent, and intrauterine infections during pregnancy are frequently subclinical and escape diagnosis. Furthermore, many intrauterine infections are caused by bacteria that resist cultivation, thus limiting the utility of culture-based detection.

Culture-independent detection methods are becoming more common and are enabling a more advanced understanding of the genetic content of the vaginal microbial community, known as the vaginal microbiome. Through the NIH's Human Microbiome Project, research is showing the vaginal microbiome to be more diverse and complex than previously suspected [81, 82]. Improvements in DNA sequencing will enable detailed characterization of these infectious bacteria. However, current knowledge of the vaginal microbiome in pregnant women is limited, and research connecting the maternal microbiome with prenatal stress and birth outcomes is in its infancy. However, there have been substantial advances attained in the characterization of the intestinal microbiome and elucidation of its relationship with the central nervous system. This progress is promising. For example, psychosocial stress has been shown to alter the composition of the intestinal microbiome. Specifically, prenatal stress in rhesus monkeys has resulted in reduced gut concentrations of lactobacilli (the most prevalent of the lactic acid-producing bacteria that dominate the vaginal flora of healthy women) in their newborn offspring [83]. Should this pattern translate to the maternal vaginal microbiome as well, it would provide important insights into the biological pathways mediating infectious causes of PTB and their relationships with the maternal nervous system's response to psychosocial stress.

In pregnant women, psychosocial stress is thought to modulate the immune response. Inflammatory and infectious pathways to PTB are linked together, as the immune and inflammatory

responses influence each other reciprocally. In cases of infection, the inflammatory response serves to initiate an immune response to control the infection.

Neuroendocrine pathways

The maternal HPA axis constitutes the principal neuroendocrine mechanism mediating the link between PSP and PTB [13]. In pregnancy, maternal cortisol stimulates placental gene expression that increases placental CRH production. Although cortisol inhibits maternal hypothalamic CRH production, placental CRH production increases maternal CRH and also stimulates maternal adrenal cortisol secretion, creating a feedback loop. Ultimately, maternal CRH concentrations increase 20-fold across the course of pregnancy [16, 53], peaking at labour and delivery.

Epidemiological evidence strongly suggests that maternal cortisol is correlated with PTB [84]. Cortisol contributes to increased prostaglandin production and downregulation of prostaglandin-metabolizing enzymes, which accelerate paracrine and autocrine aspects of parturition [85, 86]. It is likely that CRH also plays a role in the association between PSP and PTB. Although it has been hypothesized that CRH is a noncausal marker for PTB [87], several plausible hypotheses suggest CRH to play a causal role in the initiation of parturition. CRH promotes fetal prostaglandin production, leading to premature myometrial contractility. In addition, CRH stimulates fetal and steroid hormone output, leading to placental estrogen biosynthesis and subsequent myometrial activation [88]. CRH is also linked with activation of the fetal HPA [71], leading to uterine activation [85]. Of note, CRH measurements have been able to distinguish patients presenting in preterm labour who deliver preterm from those who go on to deliver at term [88, 89], suggesting that term and preterm birth have differing neuroendocrine underpinnings.

PSP, CRH and PTB

CRH is one mechanism hypothesized to function as a “placental clock” controlling parturition, and CRH trajectories across pregnancy have predicted timing of delivery [90]. There is some evidence

linking PSP with maternal CRH. Although the precise links among maternal stress, CRH, and parturition remain unclear, an emerging body of research has begun to explore these relationships and to advance and test hypotheses regarding neuroendocrine mechanisms connecting PSP and PTB.

In one study, at 28-30 weeks' gestation, the effect of pregnancy-related anxiety on gestational age became nonsignificant after controlling for CRH level, that is, CRH appeared to mediate the relationship between anxiety and gestational age at delivery [91]. However, other studies have failed to find associations between stress or anxiety and maternal CRH. One study of women in mid-pregnancy found job stress and stressful life events were unrelated to serum CRH at 28 weeks' gestation [92]. An additional study found an association between perceived stress and PTB; however, perceived stress was unrelated to maternal CRH as measured at the second trimester [62].

In contrast to these negative findings, moderating effects have been observed between stress and CRH on PTB in two studies. In one study, Guendelman et al. [93] found that the effect of CRH on preterm delivery was stronger in women exposed to chronic stressors during pregnancy compared with unexposed women. In a second study, Hobel et al. [58] compared women delivering preterm with matched term deliveries, finding a positive association between perceived stress and maternal plasma CRH for the PTB cases but a negative association for controls. Interestingly, stress was also inversely associated with CRH in the study by Guendelman et al. [93], who hypothesized that reduced CRH may be a protective response on the part of the placenta to prolong gestation in cases of stress.

Taken together, these results suggest that CRH does not consistently mediate or modify the association between PSP and PTB. However, as both psychosocial stress and elevated CRH levels and rates of increase across pregnancy have been frequently associated with PTB, it is likely that psychosocial stress interacts with maternal CRH to shorten gestation in some cases. The studies by Guendelman et al. [93] and Hobel et al. [58] provide preliminary support for this hypothesis.

Limitations

Several relevant exposures fall outside the scope of this review. As discussed above, we did not include clinical anxiety disorders in our discussions of maternal anxiety. We also did not delve into research examining the role played by maternal age in PTB, and we did not examine several other diverse types of stressors such as occupational stress and oxidative stress. Studying the links between these forms of stress and PTB requires substantially different tools and study designs from the research targeted by our review. Finally, we did not examine the impact of depressive symptoms or clinical depression. Although anxiety and depression bear some overlapping features, they are separate conditions, both at clinical and subclinical levels. As several studies have found anxiety and depression are most likely to impact on pregnancy outcomes when comorbid [94, 95], future research on clinical and subclinical levels of these conditions during pregnancy should clarify their independent and synergistic effects.

Summary and Future Directions

PTB is a significant and growing public health problem entailing substantial medical, social, and economic costs. Despite steady scientific progress leading to improved understanding of its risk factors and underlying physiology, PTB rates have not declined and are in fact increasing globally. A robust and growing body of research supports the role of psychosocial stress as an etiological risk factor for PTB. Set against a context of poor prediction coupled with increasing incidence of PTB, the importance of psychosocial stress is further highlighted by its potential amenability to intervention. Psychometric research has made significant advances in identifying the most sensitive tools to measure PSP, while clinical research has begun elucidating the interlocking biological pathways connecting PSP with PTB. In reviewing the current knowledge base on PSP and PTB and the role played by neuroinflammatory,

infectious, and neuroendocrine pathways in this relationship, several major findings and promising future research directions emerge.

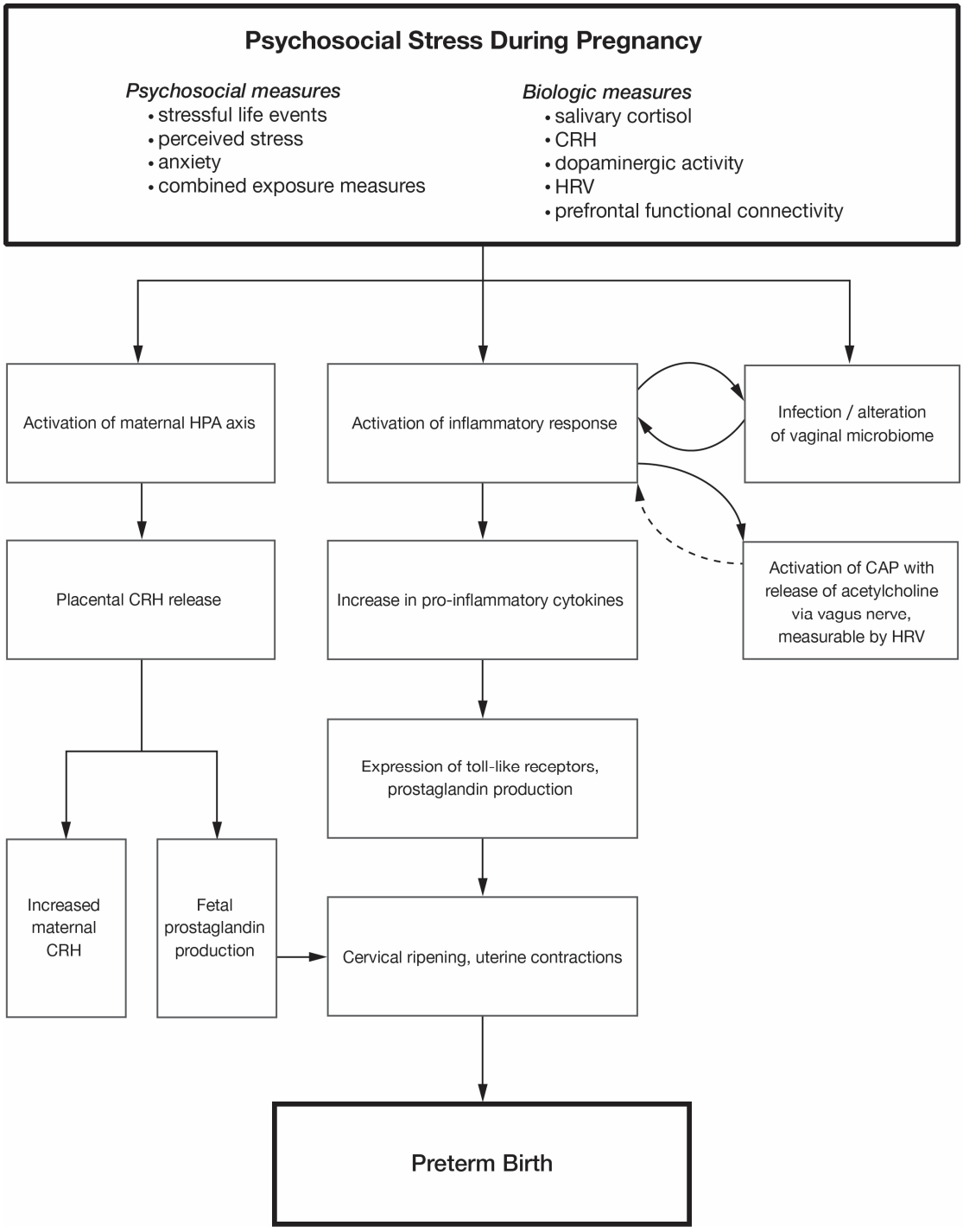
Research to date on PSP has used many related and overlapping stress and anxiety measures. Although trait anxiety could have protective effects against PTB, perceived stress and pregnancy-related anxiety appear to be the stress measures most consistently associated with risk for PTB. These findings support the study of prevention strategies aimed specifically at pregnancy-related anxiety and perceived stress in randomized clinical trials of prenatal intervention programs. To continue informing such efforts, future research must study these exposures and their reduction at multiple time points across pregnancy.

Further work is also needed to clarify the role played by maternal age-related stressors. Associations have been observed between PTB and both extremely low and high maternal age [96, 97], and research on stress and birth outcomes tends to treat maternal age as a potential confounding variable. It is readily plausible that maternal age could be associated with some forms of psychosocial stress and that stress may therefore be a mediating pathway that accounts for some of the link between maternal age and PTB. However, research to date has not distinguished the roles played by biological age, previous pregnancies and family stresses. Future work exploring age-related stressors in pregnancy will need to use study designs that take into account these factors.

Neuroendocrine biomarkers including cortisol and CRH provide important insights into the role of the neuroendocrine system in the initiation of parturition and the relationship between PSP and PTB. Inflammation and infection are other key mediating factors in this relationship. Although these physiological pathways have not conclusively explained the connection of psychosocial exposures to PTB, several novel advances show considerable promise in this area. For example, the ability to monitor CAP activity via HRV presents an exciting possibility for the safe and inexpensive exploration of the link between stress and inflammation and the role of inflammation in term and preterm parturition.

Characterization of the structure and function of the maternal microbiome will enable a clearer and richer understanding of the role played by infection in the relationship between stress and length of gestation. Research joining the fields of psychometrics, epidemiology, and clinical obstetrics points toward promising possibilities for future interventions to prolong gestation where appropriate and reduce the rate of PTB.

Figure 1. Key physiologic pathways connecting PSP to PTB



Solid arrows = known or hypothesized causal relations; solid curved arrows = positive feedback loops; dashed arrows = negative feedback loops.

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Information sur l'article

Chapitre 3 : Psychosocial Stress in Pregnancy and Preterm Birth: Associations and Mechanisms

Titre de l'article : Psychosocial stress in pregnancy and preterm birth: associations and mechanisms

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Depuis la publication de notre deuxième revue de littérature, des études poursuivent l'examen des liens entre le SPG et la NP. Plusieurs ont trouvé des liens faibles ou seulement chez des sous-groupes de la population étudiée. Par exemple, une étude portant sur un groupe de 920 femmes afro-américaines ou latino-américaines a trouvé une association significative mais faible (OR = 1,06 ; 95 % CI = 1,01 ; 1,10) entre le stress lié à la grossesse au troisième trimestre et la NP [171]. Une étude canadienne, qui a défini le stress psychosocial cumulatif comme une combinaison d'un état anxieux pendant la grossesse et d'autres troubles de santé mentale, a pour sa part trouvé que cette variable était un facteur de risque significatif pour la NP entre 34 et 37 semaines (OR = 1,7 ; 95 % CI = 1,1 ; 2,8), alors que l'association avec la NP extrême (<34 semaines) n'était pas statistiquement significative (OR = 2,4 ; 95 % CI = 1,0 ; 6,3) [172]. Une autre étude de cohorte récente a trouvé une association significative entre le stress post-traumatique et la NP dans les analyses de données brutes, mais celle-ci n'a persisté que dans les analyses ajustées chez les femmes ayant également eu un épisode majeur de dépression [173]. Au Pérou, une étude cas-témoin a trouvé un rapport significatif entre des évènements stressants de la vie pendant la grossesse et la NP (OR=2,2 ; 95 % CI = 1,7 ; 2,9) [174], tandis qu'une autre étude américaine sur une cohorte de 169 femmes, dont l'intérêt était centré sur l'affect positif, mais qui a aussi examiné le stress perçu comme covariable, n'a pas trouvé de relation significative entre le stress prénatal perçu et la durée de gestation ou la NP [175]. Des résultats équivoques ont même été observés dans les populations à risque élevé. Par exemple, dans une étude de cohorte sur des femmes à faible revenu aux États-Unis, le stress prénatal perçu n'était pas associé avec le travail prématuré (OR = 1,1 ; 95 % CI = 0,7 ; 1,8), alors qu'un lien approchant de la signifiance statistique a été observé avec la NP (OR = 1,5 ; 95 % CI = 1,0 ; 2,2) [176]. Le prédicteur le plus fort de la NP était une NP antérieure.

L'ensemble de cette littérature pose les bases de notre investigation sur les liens entre le SPG et la NP au sein de la cohorte 3D. Le prochain chapitre constitue pour sa part l'analyse principale de la thèse. Dans le sous-échantillon de la cohorte comprenant les accouchements spontanés, nous

utiliserons des mesures du SPG lors des trois trimestres de grossesse pour mesurer les relations entre quatre formes de SPG et la durée de la gestation. Nous examinerons également le rapport entre le SPG et la NP spontanée avant 37 semaines de grossesse, ainsi qu'avec la naissance spontanée avant 39 semaines.

Chapter 4

Psychosocial Stress during Pregnancy and Length of Gestation in the 3D Cohort Study

Abstract

Background: While preterm birth (PTB) is a problem of great public health concern, its determinants are not well explained. There has been heterogeneity in findings regarding the role of various forms of psychosocial stress during pregnancy (PSP) as a potential predictor of PTB. Reviews have identified several factors that may account for this heterogeneity, including stress measures used, timing of stressors during pregnancy, demographic characteristics, and clinical cutoffs for PTB. To clarify heterogeneous findings of previous literature, four forms of psychosocial stress across pregnancy were examined in association with length of gestation to test the following hypotheses: 1) among pregnancy stress measures, pregnancy anxiety and perceived stress would exhibit the strongest relationships with length of gestation; 2) stress measures in the first trimester would have the strongest association with length of gestation; and 3) PSP would be most strongly associated with length of gestation among women of lower socioeconomic status and those from minority racial groups.

Methods: Using a large pregnancy cohort (3D Cohort Study) of 2366 women in Québec, Canada, three of the psychosocial stress measures (general perceived stress, pregnancy anxiety and stress in the partner relationship) were assessed following prenatal study visits in each trimester of pregnancy, and stressful life events were measured in the second trimester only. Gestational age at birth was estimated from the last menstrual period and ultrasound data collected from a post-partum chart review.

Results: Spontaneous labour onset or spontaneous rupture of membranes leading to a live birth was found in 1585 participants. The mean length of gestation was 39.3 weeks. There were 105 spontaneous preterm births (6.6%) and 355 spontaneous early term (37 - <39 weeks) births (22.4%). After controlling for confounders and testing for moderators in multivariate regressions, only third-

trimester pregnancy anxiety was statistically associated with length of gestation, but the magnitude of the effect was small. Third-trimester pregnancy anxiety was also associated with spontaneous birth before 39 weeks (OR for one standard deviation increase = 1.13, 95% CI = 1.00-1.26). None of the stress measures showed evidence of associations with spontaneous preterm birth in multivariate analyses. There were no moderating effects of income, education, minority racial group, or parity.

Discussion and conclusions: We found no evidence to support the hypothesis that psychosocial stress is a clinically significant contributor to risk of PTB or reduced length of gestation. This conclusion is strengthened by our use of a range of psychosocial stress measures administered at three time points in pregnancy, thus overcoming several limitations of previous research.

Introduction

Preterm birth (PTB; birth before 37 weeks completed gestation) is one of the most widespread [1-4] and growing [3-6] public health issues in the perinatal field. The pathophysiology of PTB has been better understood in recent years [7-9], but prediction remains troublingly poor [7, 10]. Alongside exploration of the biological underpinning of preterm parturition, research into the psychological factors connected to PTB has expanded [11-13]. Established predictors of PTB include demographic characteristics such as single marital status, younger or older maternal age, racial identification, and smoking [4]. Aspects of pregnancy history including previous PTB [4, 14, 15], stillbirth [16], and spontaneous or induced abortion [14, 16]) are also important predictors. Following on a rich body of work describing the biological manifestations and sequelae of psychosocial stress during pregnancy (PSP) [17-20], the relationship between PSP and PTB has also become a topic of substantial interest [10, 11, 21-26]. It has been proposed that stress (particularly perceived stress) is one of the pathways connecting sociodemographic characteristics and PTB [13, 27, 28]. However, this hypothesis has received little systematic investigation, and research to date on the relationship between PSP and length of gestation has produced mixed results [22, 29]. Some studies have found significant positive associations between PSP and PTB. One study found a significant adjusted odds ratio of 1.8 [30], while other studies found relative risks ranging from 1.2 to 2.9 [31-34]. Some studies have found significant associations only among subgroups of the population examined (specific racial groups) [35, 36], and negative findings have also been observed [37-39] (non-significant ORs ranging from 0.8 to 1.6). These negative findings do not seem to be due to a lack of power, as these studies had samples of similar size to those with positive findings.

It is likely that the heterogeneity of results in this area is partly due to the varying ways in which PSP is conceptualized and measured [10, 22, 26, 40]. In fact, two meta-analyses looking at psychosocial stress and perinatal outcomes [23, 41] found that the links between PSP and outcomes were small

overall (r = -.04, 95% CI -.08 to -.01, 35 studies [23]; Cohen's *d* = -.02, 95% CI -.031 to -.004, 51 studies [41]) but varied as a function of the stress measure used. One of the meta-analyses found that significant associations were confined to measures of perceived stress (*d* = -0.06, 95% CI -0.09 to -0.02, 33 studies) and pregnancy anxiety (*d* = -0.16, 95% CI = -0.26 to -0.06, 8 studies), with no significant associations found for trait anxiety or objective life event stress [41]. Interestingly, this study also found that significant associations were confined to studies performed in the United States (*d* = -0.06, 95% CI -0.09 to -0.03, 32 studies), with no significant associations observed for studies from Europe (17 studies) or elsewhere (2 studies). The second meta-analysis found that PSP exhibited a stronger relationship with perinatal outcomes in samples with more participants from ethnic minorities [23]. Effect sizes also varied by the study design and quality [42], with stronger associations observed in studies receiving higher quality ratings and in those with a cohort rather than a case-control design [23].

Among factors that may explain heterogeneity, biological evidence lends plausibility to a moderating effect of socioeconomic status in the relationship between stress and shortened gestation, psychosocial stress exhibiting stronger effects on inflammation among participants of low socioeconomic status as defined by employment grade [43] and among African American women [44]. Further, studies of environmental disasters have consistently shown that the timing of exposure moderates the effects of traumatic events during pregnancy, with significant effects more often observed for exposure early in pregnancy [45-48]. Finally, there is some evidence that timing of exposure may also moderate the effects of less severe stressors in pregnancy [49].

We also note that studies of the impact of stress on length of gestation have operationalized the study outcome in various ways, with some studies looking at gestational age continuously and others looking at PTB categorically. While a cutoff of 37 weeks has traditionally served as a clinical endpoint in studies looking at length of gestation, evidence suggests that risk of neonatal morbidity and mortality is lowest for infants born at 39 weeks gestation or more [50-53]. Accordingly, it may be valuable to

consider preterm (<37 weeks) along with early term (37 to 39 weeks) births together as an alternative clinical endpoint [54]. Alternatively, it has been suggested that these clinical cutoffs do not clearly separate high- from low-risk births [52, 55-57]. It is therefore plausible that the use of these different outcome measures has also contributed to the heterogeneity of findings in this literature.

In summary, the existing literature examining the link between PSP and length of gestation suggests that overall associations are likely to be small and may be moderated by aspects of study design, study population, and exposure and outcome measurements used. Indeed, previous studies in this area have been limited by small sample sizes [58-61], use of a single stress measures [62-64], measurement of stress at only one [17, 30, 33, 35, 63, 65-69] or two [32, 34, 38, 60, 64, 70] time points during pregnancy, use of objective as opposed to subjective measures of stress [32, 68], and examination of only a single dichotomous outcome [60, 68]. We sought to address these limitations using data from a Canadian pregnancy cohort. Our objectives were: 1) to describe the associations between four forms of PSP and length of gestation in pregnancies ending in a spontaneous live birth; 2) to determine which aspects of PSP best predict shortened gestation; 3) to determine when in the pregnancy psychosocial stress exerts the strongest associations with length of gestation, and 4) to measure the associations between our predictors and two dichotomized clinical endpoints: a) spontaneous PTB (before 37 weeks), and b) spontaneous preterm or early term birth (before 39 weeks). Those objectives served as a background to test the following hypotheses: 1) that, among pregnancy stress measures, pregnancy anxiety and perceived stress would exhibit the strongest relationships with length of gestation, and 2) that stress measures in the first trimester would have a stronger association with length of gestation than stress in later trimesters. Further, we expected 3) that PSP would be most strongly associated with length of gestation among women of lower socioeconomic status (education and family income), and among participants from minority racial groups.

Methods

Study sample and data collection

The 3D Cohort Study comprises 2366 women recruited during the first trimester of pregnancy at one of 10 clinical centres in the province of Québec, Canada. Women were between 18 and 45 years of age at the time of recruitment and fluent in English or French. Exclusion criteria included current illegal drug use, severe illnesses or life threatening conditions, and multiple gestation pregnancies. The sample comprised 42% of 5669 eligible women approached, and 26% of 8974 women approached overall.

Demographics, gestational age at delivery and other pregnancy measures

Data on maternal demographic characteristics and medical history including outcomes of all previous pregnancies were collected using an interviewer-administered questionnaire at study entry. Variables examined include maternal age at study entry (<25, 25-29, 30-34, ≥35), parity (1, 2, >2), annual household income in Canadian dollars (<30,000, 30,000-49,999, 50,000-99,999, ≥100,000), maternal education level (less than college, college or technical school, university degree, master's or doctoral degree), maternal self-reported race (white or other), country of mother's birth (Canada or other), marital status (married or living with a partner vs. not married/living with a partner), smoking status (never, former, or current smoker), employment status (full time, part time, student, unemployed, housewife or other), pre-pregnancy BMI (<18.5, 18.5-24.9, 25-29.9, ≥30), gestational weight gain (GWG) according to the US Institute of Medicine guidelines [71], and vaginal bleeding in the first trimester. Previous adverse pregnancy outcomes measured included PTB, miscarriage, stillbirth and elective abortion. Gestational age at birth was measured from a chart review at delivery and was estimated based on from the last menstrual period and ultrasound data [72]. In accordance with recommendations [73, 74], spontaneous birth was defined as either vaginal or caesarean birth following spontaneous labour or spontaneous rupture of membranes.

Measures of psychosocial stress

Four forms of psychosocial stress were measured using self-administered questionnaires. General perceived stress, pregnancy anxiety and stress in the partner relationship were assessed following three prenatal study visits (8-14 weeks, 20-24 weeks, 32-35 weeks), while stressful life events were assessed in the second trimester only.

Perceived stress was assessed using the short form of the Perceived Stress Scale (PSS) [75]. This instrument asks how often an individual has felt about non-specified stress over the past week, with responses rated on a Likert-type scale with a range from 0 to 4. The four items ask the respondent how often over the past 7 days she felt "unable to control the important things in your life," "confident in your ability to handle your own personal problems," "that things were going your way," and "that difficulties were overwhelming." Initial psychometric testing showed a Cronbach's α reliability estimate of .72 and a test-retest correlation of .55 [75], while validation in a pregnant population produced a Cronbach's α coefficient of .79 [76]. Cronbach's α coefficients in our data ranged from .75 to .78.

Stressful life events occurring from the beginning of pregnancy through the second-trimester questionnaire administration were measured using the 17-item Prenatal Life Events Scale [59]. This instrument measures the occurrence of events such as moving, change in family or living status, natural disasters, and experiences of discrimination. In addition, the perceived impact of each event experienced by the individual is rated on a 4-point scale from 0 to 3. We computed the number of life events reported as well as the mean perceived impact for all events reported. Participants reporting no stressful life events were assigned a perceived impact score of zero.

We measured pregnancy anxiety using a four-item scale developed by Dunkel-Schetter and colleagues [77]. The items are scored on a Likert-type scale from 0 to 4 and measure anxious feelings, concerns, fears, and panic over the last week about being pregnant. Cronbach's α coefficients for this

scale ranged from .67 to .72 in psychometric testing [49] and were .83 at each of the three trimesters in our data.

Strain in the partner relationship was measured using one item from the Quality Marriage Index (QMI) [78] eliciting the general degree of happiness vs. unhappiness felt by an individual in her relationship with her husband or partner, as assessed by a 0-6 Likert scale. The QMI is intended to measure an individual's global assessment of his or her partner relationship [79]. The single item used in our study on general happiness in the partner relationship showed correlations with the other items in the QMI ranging from .69 to .77 [78]. Correlations between this item and total scores on the Dyadic Adjustment Scale [80] ranged from .67 to .73 [81].

Statistical analyses

All analyses were carried out using IBM-SPSS for Windows version 21 (IBM Corporation, Armonk, NY, 2012). We began by describing the demographic and clinical characteristics of the study sample using frequency distributions. We compared the length of gestation across different strata of the sample using one-way analysis of variance performed with UNIANOVA, which is robust to unbalanced designs. We also computed bivariate correlations between continuous demographic characteristics, measures of psychosocial stress at each of the three trimesters, and length of gestation. We tested each of the psychosocial stress measures at each trimester separately in order to determine if the strength of associations with length of gestation varied according to type of measurement (hypotheses 1 and 3) or timing of measurement (hypothesis 2).

For stress measures showing significant bivariate associations with length of gestation, or stress measures thought to be moderated by sociodemographic variables, linear regression models were constructed to examine these relationships with adjustment for potential confounding variables. We considered potential confounding variables that are known risk factors for PTB and plausibly associated with stress. These included clinical (parity, pre-pregnancy BMI, gestational weight gain, first-trimester

vaginal bleeding, previous adverse pregnancy outcomes) and sociodemographic (household income, maternal education, self-reported race, country of birth, marital status, employment status) characteristics, as well as smoking. To facilitate comparisons of results between different stress scales, all stress measures and continuous demographic variables were standardized prior to adjusted analyses. Missing data were imputed for regression analyses using the SPSS multiple imputation procedure, with the fully conditional specification algorithm and 5 imputations. This provides estimates of adequate precision given the rates of missing data in our study [82-84]. All exposure variables and covariates were used to create the imputed data sets. In order to avoid developing over-adjusted models and clearly describe any overlapping variance change following the inclusion of potential confounders, we ran partially adjusted models in which we did not adjust for income, education, race, or country of mother's birth. We then included these variables when developing the fully adjusted models. We tested whether socioeconomic status (household income or maternal education), maternal race or country of birth moderated associations between stress and birth outcomes (hypothesis 3) by constructing regression models that included these centered variables and their multiplicative interaction terms with the stress measures. We also tested for moderation by parity, which has been shown to moderate the effects of other PTB risk factors including maternal age [85] and smoking [86]. Finally, in order to address our fourth objective, logistic regression models were constructed to assess the relationships between psychosocial stress levels and clinical outcomes (spontaneous PTB at <37 weeks and spontaneous preterm or early term birth at <39 weeks).

Results

Study sample and psychosocial stress levels

Of the 2366 women who participated in the 3D Cohort Study, 2317 had complete data on pregnancy outcome and 2211 of these had a live birth (95%). Of the 106 participants without a live birth,

there were 19 stillbirths, 3 elective abortions, 19 therapeutic terminations of pregnancy, 2 molar pregnancies, and 63 spontaneous abortions. 1585 of the 2211 live births followed spontaneous labor onset or spontaneous rupture of membranes (72% of live births), while 626 followed induced labour or were caesarean births without spontaneous labour (28%). The 1585 participants with spontaneous live birth formed our study sample. Mean length of gestation for pregnancies in the sample was 39.3 weeks (SD = 1.8 weeks), and there were 105 spontaneous preterm births (6.6%) and 355 spontaneous early term births (22.4%).

Table 1 shows categorical demographic variables and other characteristics of the study sample, along with the average length of gestation in each stratum. More than half the women in the study sample were above the age of 30, more than half were primiparous, and more than 70% had an annual household income of at least $50,000. Only 14.6% of the study sample had a before taxes household income below Statistics Canada's before-tax low-income cut-off for their family size [87], which is in keeping with the 2010 national norm of 13.7%. Roughly one third of participants identified as being from a minority racial group, and one third were born outside Canada. 95% of women were married or living with a partner, and the majority worked full time. Correlations between the continuous values of maternal age, household income, and education level are presented in Table 2.

Across both tables, significant correlates of lower gestational age were as follows: Lower levels of maternal education and household income, non-white race, birth outside Canada, lower GWG, and first-trimester vaginal bleeding. The average length of gestation for women having a previous preterm birth or stillbirth was more than one week shorter than for those without. The mean length of gestation was also slightly shorter among women with a prior elective abortion. The omnibus F-test showed variation in length of gestation by smoking status, and post-hoc comparisons using the Tukey HSD test revealed significantly shorter length of gestation among current smokers or never smokers compared to former smokers ($p < .05$).

Response rates to the self-administered questionnaires from which PSP was measured varied from 77% at the first trimester to 70% at the third trimester. Data were missing more frequently for participants with lower household incomes or education levels and from racial minorities. The overall response rates were 59% and 60% for participants in the lowest household income and education categories respectively, whereas they were 80% in the highest categories. Response rates were 78% for participants identifying as white and 62% for non-white participants.

The maximum number of stressful life events reported was 7 out of a possible 17. The psychosocial stress levels spanned the full possible range of all other scales (0 to 16 for perceived stress and pregnancy anxiety, 0 to 6 for strain in the partner relationship, 0 to 3 for perceived impact of life events). For the stress measures taken at all three trimesters, mean levels ranged from 3.3 (SD = 2.7) to 3.8 (3.0) for perceived stress, 3.0 (2.9) to 3.6 (3.2) for pregnancy anxiety, and was 1.5 at all three trimesters for marital strain (SDs ranged from 1.1 to 1.2). Mixed model analysis showed that perceived stress was significantly higher in the first trimester compared to the second and third trimesters, and that pregnancy anxiety was highest in the first trimester and lowest in the second trimester, with significant differences between all three measurements. Marital strain did not vary significantly across the three trimesters. The mean number of life events reported from the beginning of pregnancy through the second trimester visit was 1.1 (SD = 1.2), and the mean reported impact of life events was 0.8 (1.0).

Bivariate correlations between psychosocial stress and length of gestation

Table 2 shows the crude bivariate correlations prior to imputation among continuous demographic variables, length of gestation and psychosocial stress measures at each trimester for pregnancies ending in a spontaneous birth. Intercorrelations among stress measures ranged from .04 to .61, with a median correlation of .22. Intercorrelations were highest within measures across trimesters and lowest across measures between marital strain and pregnancy anxiety. Perceived stress in the third trimester and pregnancy anxiety in the first and third trimesters were each weakly but significantly

correlated with shorter gestation (hypotheses 1 and 2), while marital strain and stressful life events were not significantly associated with length of gestation (hypothesis 1).

Adjusted analyses

Table 3 shows results of multivariable linear regression models examining the adjusted effects on length of gestation of those stress measures that showed significant bivariate associations (third-trimester perceived stress and pregnancy anxiety in the first and third trimesters). Of the psychosocial stress measures, only third-trimester pregnancy anxiety was significantly associated with length of gestation in adjusted analyses (hypotheses 1 and 2). Length of gestation was decreased by 0.09 weeks for each standard deviation increase in the pregnancy anxiety scale in the third trimester. Finally, none of the stress measures significantly interacted with income, education, race or country of birth to predict length of gestation (hypothesis 3), nor were there significant interactions between stress and parity. The roles of covariates were as follows: In the partially adjusted models, previous preterm birth and first-trimester vaginal bleeding were associated with shorter gestation, and GWG was associated with longer gestation. In the fully adjusted models, higher maternal education was also associated with longer gestation. Non-white race was associated with shorter gestation in the model for first-trimester pregnancy anxiety, while associations between racial identification and length of gestation were not significant in the other models.

Tables 4 and 5 show results of logistic regression models examining the associations between psychosocial stress and dichotomized clinical outcomes. Perceived stress in the third trimester and pregnancy anxiety in the first and third trimesters showed small associations with spontaneous birth before 39 weeks, with odds ratios ranging from 1.12 to 1.14 (Table 5). The association between third-trimester pregnancy anxiety and spontaneous birth before 39 weeks retained statistical significance after adjustment for confounding variables (OR = 1.13, 95% CI = 1.00-1.26, p=.04, Table 5). There was no other significant association between PSP and spontaneous preterm birth (Table 4) or with spontaneous

preterm or early term birth (Table 5). Here also, none of the stress measures significantly interacted with income, education, race or country of birth to predict spontaneous preterm or early term birth (hypothesis 3).

Alternative modeling strategies

Our principal analyses were conducted using linear and logistic regression, with models run separately for different stress measures at each time point. This represents one of the most simple and straightforward modeling strategies, and we arrived at this approach after exploring several other possibilities. A small body of evidence suggests that birth outcomes may be more sensitive to changes in stress levels across pregnancy than to stress per se. After completing our literature review and preliminary analyses on the exposure data in the 3D Cohort Study, we found that the evidence did not strongly suggest that variation in stress across pregnancy would display important relationships with length of gestation. This may have been due, in part, to the low overall variation in exposures across pregnancy and to the fact that exposure data were consistently left-skewed and largely confined to a narrow range of values. Nevertheless, we explored alternative modeling strategies including path analyses looking at differences between stress levels at the three time points, regression models where stress scores were averaged across the entire pregnancy, regression models with chronic stress defined as elevated scores for at least two time points or for all three time points, and stratification of participants based on modeled trajectories across the three time points [88]. None of these approaches produced stronger results than those obtained from the simpler regression models. Using these alternative exposure definitions and models, we did not observe clinically important associations between stress and length of gestation. We therefore opted to use regression models run separately for each exposure time point.

We also explored alternatives in terms of outcome variables. From an etiologic perspective, mechanisms connecting stress to length of gestation are likely to differ for indicated vs. spontaneous

births, and it is recommended that data modelling in this area distinguish between the two [89]. Nevertheless, limiting our principal analyses to spontaneous births effectively reduced our sample size by close to 30%. As an exploratory step, we ran regression models on the full cohort, with both induced and spontaneous births. Again, we did not find evidence of clearer associations than when outcomes were limited to spontaneous births.

Discussion

In this study using primary data from a large prospective cohort, we examined associations between several measures of PSP and length of gestation for pregnancies ending in a spontaneous birth. Based on previous meta-analyses [23, 41], we hypothesized that pregnancy anxiety and perceived stress would exhibit the strongest relationships with length of gestation, and that stress measured in the first trimester would be more strongly correlated with length of gestation than stress in later trimesters. We found that third-trimester perceived stress and first- and third-trimester pregnancy anxiety were weakly associated with length of gestation in crude analyses. While the association with third-trimester pregnancy anxiety retained statistical significance after adjusting for previous preterm birth, GWG, first-trimester vaginal bleeding, maternal education and self-reported race, it was not of a clinically meaningful magnitude; an increase of one standard deviation in the pregnancy anxiety score (about 3 points on a 0-16 scale) represents a substantial jump, whereas the corresponding point estimate of -0.09 weeks represents roughly 15 hours of gestation. Contrary to expectations, there were no stronger links between PSP and length of gestation among women of lower socio-economic status, those from racial minority groups, or as a function of parity. We observed an association of borderline statistical significance between third-trimester pregnancy anxiety and spontaneous birth before 39 weeks, but there were no other statistically significant associations between PSP and dichotomous clinical endpoints.

As has been demonstrated in other studies, previous PTB [90-92] and first-trimester vaginal bleeding [6, 93, 94] were strong predictors of shortened gestation. Women in our study who had previously given birth to a preterm infant had more than double the odds of spontaneous PTB in the study pregnancy and more than triple the odds of spontaneous birth before 39 weeks. The effect sizes for clinical variables in comparison to the stress variables we examined help put into perspective the role played by psychosocial stress in determining length of gestation.

Our hypotheses were designed to clarify much heterogeneity of findings reported in previous literature. We did not observe strong associations of PSP on PTB, as some other studies have [31, 33]. The strongest associations that we did find with length of gestation as measured continuously were for perceived stress and pregnancy anxiety, as expected. Our investigation of spontaneous birth before 39 weeks represents a less-commonly studied clinical endpoint, but one that is nevertheless important in terms of neonatal developmental outcomes. Our study suggests a slightly increased risk of spontaneous preterm or early term birth associated with higher third-trimester pregnancy anxiety. This finding makes a novel contribution to the literature on psychosocial stress and birth outcomes, as little research has measured associations between stress and early term birth. Our study suggests this may be an important endpoint to examine in future research. Thus, our study makes an important contribution to the literature in that, despite the large sample size and having tested some of the putative moderators thought to cause heterogeneity across several study findings, it fails to reveal a clinically important association between any of the four stress measures and length of gestation or PTB. It does however demonstrate an effect of third-trimester pregnancy anxiety on the risk of spontaneous birth before 39 weeks.

A great deal of attention has justifiably been devoted to the study of PSP and its links with pregnancy outcomes [10, 21, 22]. Numerous studies have found significant associations between PSP and PTB [30, 31, 33-35, 63]. Evidence from animal models supports physiologic links between PSP and

PTB [95, 96], and correlations between stress biomarkers and PTB have been observed in human studies [97-100]. However, it has been suggested that the relationship between PSP and birth outcomes such as PTB and low birth weight may not be clinically meaningful [23], a proposition supported by our overall results. Interventions aimed at reducing stress have not generally succeeded in preventing PTB [101, 102], although several trials have shown beneficial effects in high-risk subgroups of the populations studied [103-105]. It has been noted that social support intervention trials have generally not been designed using a conceptual framework in which the intervention was targeted to a specific stressor or individual predisposition [101]. Our results suggest that it may be valuable to consider pregnancy anxiety in the development of stress-reduction interventions and as an outcome measure in trials of such interventions. Stress biomarkers could also serve as intermediate outcomes.

Variable selection

Although there is an assumption that stress causes clinical outcomes, the relationships between these constructs may be more complex and require careful statistical modeling and interpretation. Consequently, there are plausible situations where adjustment for some of the variables we included in our models could be inappropriate. For example, GWG is understood as a marker for nutritional status and thus for some of the underlying mechanisms causing PTB [106], and it is also plausibly related to psychosocial stress [107, 108], but the direction of causality in this relationship is unclear. GWG may therefore lie on the causal pathway between PSP and length of gestation. While GWG was significantly linked to length of gestation in our analyses, it did not substantially change the observed associations between PSP and pregnancy duration. Thus, we do not find evidence that our observed associations of PSP were inappropriately attenuated by adjusting for GWG. Secondly, to the extent that PSP may have contributed to a previous PTB, including previous PTB in our models would be inappropriate, as it would amount to adjusting for a former instance of the principal effect under investigation. Again, previous PTB displayed strong correlations with length of gestation in our study but did not substantially change

the strength of the association between PSP and length of gestation. Finally, it is readily plausible that preterm labour would lead to increases in pregnancy anxiety. To the extent that late pregnancy anxiety was caused by preterm labour in our study population, the association we observed with length of gestation would not indicate a causal relationship. We therefore repeated our analyses adjusting for preterm labour or threatened preterm labour. Results were not substantially changed.

Strengths and limitations

Our study addresses several limitations of previous work in this area, including smaller sample sizes [58-61] and measurement of stress at only one [30, 35, 63, 65-67] or two [34, 38, 60] time points during pregnancy. In addition, we assessed the subjective perception of stress for all four measures we used, thus measuring PSP in a richer manner than is frequently available in larger administrative databases [32, 109]. Finally, we were able to adjust for a large range of potential confounding variables, including extensive data on pregnancy history. As expected, length of gestation was very sensitive to these predictors. However, several limitations to our study must be acknowledged. Our population-based cohort was recruited from general prenatal clinical settings and did not exhibit an unusually high demographic, psychosocial, or medical risk profile. This stands in contrast to some previous epidemiologic studies finding associations between PSP and birth outcomes that have been conducted in higher-risk populations, particularly with respect to race [49, 63, 110] and marital status [33, 49, 63, 110-112]. It is possible that stress as measured by commonly used psychometric instruments may act to exacerbate the effects of other pre-existing sociodemographic stressors not strongly present in our study sample, and that the selection of participants for the 3D Cohort Study may have thus contributed to some of our negative findings. However, and out of concern for that potential limitation, we tested whether stress measures were moderated by sociodemographic predictors, and they were not.

Another limitation may lie in the fact that the stress levels observed in our cohort appear to be lower than those of many other observational studies, both in direct comparison with scores observed

using the same instruments we used [30, 49, 58, 98, 111, 113] and after scaling scores from longer versions of these instruments to the range of the short-form instruments we used [114-120]. For example, in comparing the stress levels in our study to those in studies using the same scales with the same scoring algorithms, the mean level on the PSS in our study ranged from 3.3 to 3.8, compared to a range of 4.0 to 6.4 in two other studies [30, 111]. Our mean pregnancy anxiety scores ranged from 3.0 to 3.6, compared to 7.8 to 8.8 found in another cohort [30]. Stress levels also exhibited less variability in our study sample than in other studies. For example, the standard deviation of our scores ranged from 2.7 to 3.0 for the PSS and from 2.9 to 3.2 on the pregnancy anxiety scale, compared to standard deviations of 3.0 to 3.3 on the PSS [30, 111] and 3.5 to 4.1 for pregnancy anxiety [30] found in other studies. Our ability to study high levels of psychosocial stress is thus limited, and it is plausible that stronger associations with our study outcomes would be observed in populations with greater stress levels or more variation in stress exposure.

Data for our study exposures were missing for up to 30% of participants, depending on the stress measure and time point of measurement. A small amount of data were missing for covariates as well. Data were missing more frequently for higher-risk participants. It is thus most plausible that any bias caused by missing data would be towards the null hypothesis and would reduce our ability to detect existing associations. We imputed missing data in an attempt to reduce such resulting bias. The multiple imputation algorithm provides more accurate estimates of precision than single imputation [83], but the validity of the procedure rests on the assumption that data are missing at random [84], which may not be the case in our study, as missingness was associated with some demographic characteristics that were themselves associated with psychosocial stress levels. Results were not substantially changed when we expanded the set of variables used to generate imputed data, but it is still plausible that the pattern of missingness depends on unobserved data and that our results would therefore still be biased.

This constitutes a limitation of our study and of the self-administered questionnaire data in the 3D Cohort Study more broadly.

Our study also did not control for false discovery rate. With 11 exposure measures and three outcome measures, it is plausible that statistically significant findings arose due to chance. Even if this is not the case, the effects we found are at most very weak. Nonetheless, our study can make an important contribution to future meta-analyses because it looked at a more comprehensive range of exposures than much of the existing research and it tested for plausible moderating effects.

A potential criticism of our analysis is that we may have been over-adjusting for some of the demographic variables we considered as potential confounders. Women of lower socioeconomic status [14, 16, 121-123], unmarried women [124-126], and women from racial minority groups [127-130] are known to have elevated risks of PTB. These characteristics were also associated with higher levels of psychosocial stress [115, 131-133]. Socioeconomic variables are unlikely to be substantially affected by PSP within the timeframe of pregnancy, thus they would not lie on the causal path between PSP and pregnancy outcome. However, it is plausible that socioeconomic characteristics act as a common cause of both stress and adverse pregnancy outcomes. In fact, stress has been proposed as a pathway to explain socioeconomic and ethnic disparities in perinatal health [134, 135]. For this reason, we presented results from both the partially and fully adjusted models. To the extent that these socioeconomic characteristics were common causes of the exposure and outcome, their inclusion in the models would constitute over-adjustment. The ORs for stress variables were essentially unchanged between the partially and fully adjusted models, indicating that while maternal education and race predicted the study outcomes, the principal associations under investigation were not substantially affected by adjustment for these variables. This also suggests that measures of SES were independent predictors of length of gestation in our data, rather than functioning through the pathway of psychosocial stress.

Avenues for future research

The relationship between psychosocial and biological measures of stress is not straightforward, and combining psychosocial and biologic stress measures has been shown to improve the prediction of PTB [136]. One relatively small study (N=78) measured CRH at four time points and perceived stress at two time points during pregnancy [137] and found significantly higher CRH levels in the third trimester among women who went on to a preterm delivery. While no significant differences were found in perceived stress levels between the PTB and term birth groups, the combination of perceived stress and CRH predicted length of gestation better than CRH alone. In a second study of 282 pregnant women [98], CRH and pregnancy anxiety were measured in the second and third trimesters. In this study, CRH levels were significantly higher at both time points among women who went on to a PTB. Pregnancy anxiety in the third trimester was also significantly correlated with shorter gestation, but linear regression analyses found that this relationship was mediated by third-trimester CRH and was no longer statistically significant after controlling for CRH. Finally, a case-control study of 1094 women [99] also found that second-trimester CRH levels were significantly higher among PTB cases than among controls. In this study, the adjusted OR linking CRH to PTB was elevated among women who reported chronic stressors during pregnancy. These findings suggest that our study can be enhanced by future work combining stress biomarkers with psychosocial stress measures in the 3D cohort.

Conclusions

Based on a range of psychosocial stress measures, we observed small crude associations of perceived stress in the third trimester and pregnancy anxiety in the first and third trimesters with length of pregnancy. We did not observe clinically meaningful relationships between stress and spontaneous PTB, though we did find a weak association between third-trimester pregnancy anxiety and spontaneous birth before 39 weeks. As other studies have found, the strongest links were those for perceived stress

and pregnancy anxiety. Our study of a representative sample of the urban population in Canada is consistent with many others in that it does not provide strong evidence of a clinically important association between PSP and preterm or early term birth.

Table 1. Study sample characteristics and mean gestational age at birth in each stratum, N = 1585

		N (%)		Mean gestational age at birth (SD)	Comparison *
Maternal age	<25	120	(8%)	39.3 (1.7)	$F(3, 1576) = 1.45$, $p = .23$, $eta^2 = 0.003$
	25-29	528	(33%)	39.4 (1.4)	
	30-34	632	(40%)	39.3 (2.1)	
	≥35	300	(19%)	39.1 (1.9)	
	missing	5	(0%)	39.7 (1.0)	
Parity	1	882	(56%)	39.4 (1.9)	$F(2, 1582) = 1.60$, $p = .20$, $eta^2 = 0.002$
	2	510	(32%)	39.2 (1.7)	
	>2	193	(12%)	39.2 (1.7)	
Household income	<30,000	168	(11%)	39.2 (1.7)	$F(3, 1504) = 0.75$, $p = .52$, $eta^2 = 0.001$
	30,000-49,999	183	(12%)	39.4 (1.6)	
	50,000-99,999	685	(43%)	39.3 (1.9)	
	≥100,000	472	(30%)	39.4 (1.7)	
	missing	77	(5%)	39.2 (2.0)	
Maternal education	Less than college	167	(11%)	39.2 (1.9)	$F(3, 1546) = 4.42$, $p < .01$, $eta^2 = 0.009$
	College or technical school	386	(24%)	39.1 (2.1)	
	University degree	627	(40%)	39.4 (1.7)	
	Master's or doctoral degree	370	(23%)	39.5 (1.4)	
	missing	35	(2%)	39.0 (2.1)	
Self-reported race	White	1105	(70%)	39.4 (1.7)	$F(1, 1577) = 6.91$, $p = .01$, $eta^2 = 0.004$
	Other	474	(30%)	39.1 (2.2)	
	missing	6	(0%)	40.2 (1.5)	
Country of birth	Canada	1035	(65%)	39.4 (1.7)	$F(2, 1582) = 2.86$, $p = .06$, $eta^2 = 0.004$
	Other	545	(34%)	39.2 (2.0)	
	missing	5	(0%)	40.2 (0.4)	
Marital status	Married or living with a partner	1500	(95%)	39.3 (1.8)	$F(1, 1578) = 2.12$, $p = .15$, $eta^2 = 0.001$
	Not married or living with a partner	80	(5%)	39.0 (1.9)	
	missing	5	(0%)	40.3 (1.0)	
Smoking status	Never	926	(58%)	39.3 (1.7)	$F(2, 1403) = 5.27$, $p = .01$, $eta^2 = 0.007$
	Former	281	(18%)	39.6 (1.3)	
	Current	199	(13%)	39.2 (2.1)	
	missing	179	(11%)	39.0 (2.6)	

		N (%)		Mean gestational age at birth (SD)	Comparison *
Employment status	Full time	1088	(69%)	39.3 (1.9)	F(3, 1579) = 0.63, p = .60, eta^2 = 0.001
	Part time	140	(9%)	39.2 (2.1)	
	Student	98	(6%)	39.5 (1.5)	
	Unemployed, housewife or other	257	(16%)	39.3 (1.6)	
	missing	2	(0%)	40.5 (0.3)	
Previous preterm birth	Yes	90	(6%)	38.3 (2.1)	F(1, 1583) = 32.10, p = .00, eta^2 = 0.020
	No	1495	(94%)	39.4 (1.8)	
Previous miscarriage	Yes	338	(21%)	39.2 (2.0)	F(1, 1583) = 2.78, p = .10, eta^2 = 0.002
	No	1247	(79%)	39.4 (1.8)	
Previous stillbirth	Yes	23	(1%)	38.0 (3.1)	F(1, 1583) = 11.67, p = .00, eta^2 = 0.007
	No	1562	(99%)	39.3 (1.8)	
Previous elective abortion	Yes	280	(18%)	39.1 (2.4)	F(1, 1583) = 6.36, p = .01, eta^2 = 0.004
	No	1305	(82%)	39.4 (1.7)	
Pre-pregnancy BMI	Underweight (<18.5)	111	(7%)	39.3 (1.9)	F(3, 1500) = 1.51, p = .21, eta^2 = 0.003
	Normal (18.5-24.9)	990	(62%)	39.3 (1.7)	
	Overweight (25-29.9)	254	(16%)	39.5 (2.0)	
	Obese (≥30)	149	(9%)	39.1 (2.0)	
	missing	81	(5%)	39.1 (1.7)	
Gestational weight gain	<IOM	329	(21%)	39.2 (2.1)	F(2, 1436) = 3.94, p = .02, eta^2 = 0.005
	=IOM	521	(33%)	39.4 (1.5)	
	>IOM	589	(37%)	39.5 (1.4)	
	missing	146	(9%)	38.4 (3.2)	
Vaginal bleeding first trimester	Yes	200	(13%)	38.8 (2.6)	F(1, 1583) = 18.50, p = .00, eta^2 = 0.012
	No	1385	(87%)	39.4 (1.7)	

* Statistical comparisons do not include participants in the Missing category.

Table 2. Correlations between psychosocial stress levels and length of gestation for pregnancies ending in a live birth following spontaneous labour or spontaneous rupture of membranes, maximum N = 1585

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.
1. Age	-											
2. Household income	.18**	-										
3. Maternal education	.29**	.31**	-									
4. Perceived stress 1	-.04	-.19**	-.07*	-								
5. Perceived stress 2	-.06*	-.20**	-.07*	.53**	-							
6. Perceived stress 3	.05	-.16**	-.06	.47**	.49**	-						
7. Pregnancy anxiety 1	.00	-.08**	-.03	.41**	.33**	.32**	-					
8. Pregnancy anxiety 2	-.03	-.05	-.01	.30**	.41**	.33**	.58**	-				
9. Pregnancy anxiety 3	-.02	-.04	-.01	.30**	.32**	.43**	.52**	.61**	-			
10. Marital strain 1	.06*	-.13**	-.05	.31**	.23**	.23**	.12**	.04	.09**	-		
11. Marital strain 2	.07*	-.06*	-.04	.25**	.36**	.22**	.08**	.11**	.10**	.58**	-	
12. Marital strain 3	.12**	-.02	-.02	.17**	.22**	.33**	.12**	.08*	.14**	.53**	.58**	-
13. Stressful life events: count	-.02	-.14**	.01	.17**	.27**	.14**	.15**	.16**	.09**	.08**	.14**	.06
14. Stressful life events: perceived impact	-.01	-.02	.03	.18**	.27**	.14**	.13**	.16**	.10**	.11**	.16**	.12**
15. Length of gestation	-.06*	.04	.06*	-.03	.00	-.08*	-.06*	-.02	-.09**	.01	-.04	-.02
N	1580	1508	1556	1244	1211	1121	1244	1213	1122	1152	1109	928

	13.	14.	15.
13. Stressful life events: count	-		
14. Stressful life events: perceived impact	.56**	-	
15. Length of gestation	.00	.01	-
N	1221	1216	1585

* $p < .05$ ** $p < .01$

Table 3. Results of multiple linear regression analyses of psychosocial stress during pregnancy and length of gestation for pregnancies ending in a live birth following spontaneous labour or spontaneous rupture of membranes, N = 1585

	Crude models			Partially adjusted models			Fully adjusted models		
Exposure	**B**	**95% CI**	**p**	**B**	**95% CI**	**p**	**B**	**95% CI**	**p**
Perceived stress 3	-0.07	-0.16, 0.02	0.11	-0.05	-0.14, 0.04	.24	-0.04	-0.12, 0.05	.40
Previous preterm birth				-0.92	-1.22, -0.63	<.01	-0.93	-1.23, -0.64	<.01
Gestational weight gain				0.09	-0.01, 0.19	.08	0.11	0.00, 0.21	.04
Vaginal bleeding first trimester				-0.37	-0.58, -0.17	<.01	-0.37	-0.57, -0.16	<.01
Education							0.09	0.02, 0.17	.02
Non-white race							-0.08	-0.23, 0.07	.30
	F(1,1563)=4.50, p=0.07, R^2=.002			F(4,1560)=14.61, p<.01, R^2=.034			F(6,1558)=10.99, p<.01, R^2=.037		
Pregnancy anxiety 1	-0.11	-0.22, 0.00	0.06	-0.09	-0.20, 0.02	.11	-0.08	-0.18, 0.03	.16
Previous preterm birth				-1.10	-1.48, -0.72	<.01	-1.10	-1.48, -0.72	<.01
Gestational weight gain				0.14	0.01, 0.27	.04	0.17	0.04, 0.30	.01
Vaginal bleeding first trimester				-0.57	-0.84, -0.30	<.01	-0.55	-0.82, -0.29	<.01
Education							0.15	0.06, 0.25	<.01
Non-white race							-0.20	-0.40, -0.01	.04
	F(1,1583)=6.12, p<.01, R^2=.003			F(4,1580)=15.26, p<.01, R^2=.035			F(6,1578)=12.78, p<.01, R^2=.043		
Pregnancy anxiety 3	-0.10	-0.18, -0.03	0.01	-0.10	-0.17, -0.03	.01	-0.09	-0.17, -0.02	.01
Previous preterm birth				-0.94	-1.23, -0.64	<.01	-0.94	-1.23, -0.64	<.01
Gestational weight gain				0.09	-0.01, 0.19	.07	0.11	0.00, 0.21	.04
Vaginal bleeding first trimester				-0.38	-0.58, -0.17	<.01	-0.37	-0.58, -0.17	<.01
Education							0.09	0.02, 0.17	.02
Non-white race							-0.08	-0.22, 0.07	.32
	F(1,1563)=8.29, p<.01, R^2=.005			F(4,1560)=16.14, p<.01, R^2=.037			F(6,1558)=12.02, p<.01, R^2=.041		

Table 4. Results of multiple logistic regression analyses of psychosocial stress during pregnancy and preterm birth following spontaneous labour or spontaneous rupture of membranes, N = 1585

Exposure	Crude models			Partially adjusted models			Fully adjusted models		
	OR	**95% CI**	**p**	**OR**	**95% CI**	**p**	**OR**	**95% CI**	**p**
Perceived stress 3	0.97	0.75, 1.25	.78	0.94	0.73, 1.22	.66	0.92	0.71, 1.20	.54
Previous preterm birth				2.14	1.03, 4.46	.04	2.16	1.04, 4.52	.04
Gestational weight gain				0.86	0.62, 1.20	.37	0.84	0.60, 1.18	.31
Vaginal bleeding first trimester				1.54	0.86, 2.76	.14	1.53	0.85, 2.74	.15
Education							0.89	0.69, 1.13	.33
Non-white race							1.16	0.72, 1.87	.55
Pregnancy anxiety 1	1.04	0.82, 1.32	.73	1.02	0.80, 1.29	.89	1.00	0.79, 1.26	>.99
Previous preterm birth				2.33	1.22, 4.46	.01	2.34	1.22, 4.48	.01
Gestational weight gain				0.82	0.62, 1.09	.16	0.79	0.59, 1.05	.11
Vaginal bleeding first trimester				1.71	1.02, 2.87	.04	1.67	0.99, 2.82	.05
Education							0.83	0.67, 1.03	.09
Non-white race							1.25	0.82, 1.90	.31
Pregnancy anxiety 3	1.01	0.79, 1.29	.95	1.01	0.79, 1.28	.96	1.00	0.79, 1.27	.99
Previous preterm birth				2.09	1.01, 4.34	.05	2.10	1.01, 4.36	.05
Gestational weight gain				0.86	0.62, 1.20	.36	0.84	0.60, 1.18	.31
Vaginal bleeding first trimester				1.53	0.86, 2.74	.15	1.51	0.84, 2.71	.16
Education							0.89	0.70, 1.14	.36
Non-white race							1.12	0.70, 1.80	.63

Table 5: Results of multiple logistic regression analyses of psychosocial stress during pregnancy and birth before 39 weeks following spontaneous labour or spontaneous rupture of membranes, N = 1585

Exposure	Crude models			Partially adjusted models			Fully adjusted models		
	OR	**95% CI**	**p**	**OR**	**95% CI**	**p**	**OR**	**95% CI**	**p**
Perceived stress 3	1.13	1.01, 1.27	.04	1.10	0.98, 1.24	.11	1.07	0.95, 1.21	.23
Previous preterm birth				3.67	2.35, 5.71	<.01	3.72	2.38, 5.81	<.01
Gestational weight gain				0.89	0.76, 1.04	.13	0.87	0.74, 1.02	.08
Vaginal bleeding first trimester				1.42	1.03, 1.96	.03	1.41	1.02, 1.95	.04
Education							0.89	0.79, 1.01	.07
Non-white race							1.18	0.92, 1.51	.20
Pregnancy anxiety 1	1.12	1.00, 1.25	.05	1.10	0.98, 1.23	.11	1.08	0.97, 1.21	.16
Previous preterm birth				3.85	2.48, 5.96	<.01	3.87	2.49, 6.00	<.01
Gestational weight gain				0.87	0.75, 1.02	.08	0.85	0.73, 0.99	.04
Vaginal bleeding first trimester				1.47	1.07, 2.02	.02	1.44	1.05, 1.99	.02
Education							0.88	0.78, 0.99	.03
Non-white race							1.21	0.95, 1.54	.12
Pregnancy anxiety 3	1.14	1.01, 1.27	.03	1.14	1.01, 1.27	.03	1.13	1.00, 1.26 *	.04
Previous preterm birth				3.77	2.42, 5.88	<.01	3.80	2.44, 5.93	<.01
Gestational weight gain				0.89	0.76, 1.04	.13	0.87	0.74, 1.02	.08
Vaginal bleeding first trimester				1.44	1.04, 1.99	.03	1.42	1.03, 1.97	.03
Education							0.89	0.79, 1.01	.06
Non-white race							1.18	0.92, 1.51	.18

* 95% confidence interval: 1.004, 1.261

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Information sur l'article

Chapitre 4 : Psychosocial Stress during Pregnancy and Length of Gestation in the 3D Cohort Study

Titre de l'article : Psychosocial Stress during Pregnancy and Length of Gestation in a Representative Cohort in Québec, Canada: The 3D Cohort Study

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Le chapitre précédent a présenté une recherche empirique sur la question principale de la thèse concernant le SPG et la durée de gestation. Malgré le fait qu'aucun effet significatif entre le SPG et la NP spontanée n'a été observé, ni d'effet cliniquement significatif entre le SPG et la durée de gestation, notre étude a révélé un lien faible entre l'anxiété liée à la grossesse au troisième trimestre et la naissance spontanée avant 39 semaines de gestation. Ces résultats s'intègrent à un corpus de littérature scientifique dans lequel l'anxiété liée à la grossesse est déjà considérée comme étant un des facteurs de risque psychosociaux les plus robustes relativement aux issues de grossesse problématiques [118, 177]. Néanmoins, il n'est toujours pas certain si celle-ci agirait comme facteur causal ou plutôt comme marqueur d'autres facteurs de risque.

Comme il est commenté dans le premier chapitre, les cadres conceptuels courants dans l'ensemble des articles publiés à propos de la recherche sur le SPG et les issues de grossesse ne tiennent pas systématiquement compte des grossesses antérieures [118, 137-141]. Cela pourrait constituer une lacune importante, étant donné que les issues de grossesse problématiques peuvent avoir des répercussions néfastes sur la santé mentale de la mère pendant les grossesses subséquentes [178-184]. Le prochain chapitre s'intéresse justement à cette lacune puisqu'il consiste en une étude empirique sur les liens entre les issues des grossesses antérieures et l'anxiété maternelle pendant une grossesse subséquente à l'intérieur de la cohorte 3D. Cette section vise à examiner de quelle manière l'anxiété liée à la grossesse peut refléter les facteurs de risque sous-jacents qui ont déjà été décelés lors de grossesses précédentes. Nous tentons ainsi de ramener les sentiments d'une femme concernant sa grossesse actuelle dans le cadre plus large de ses antécédents obstétricaux.

Chapter 5

Previous Pregnancy Outcomes and Subsequent Pregnancy Anxiety in the 3D Cohort Study

Abstract

Background: Pregnancy anxiety has generated substantial interest as a potential predictor of adverse pregnancy outcomes. Better understanding of the upstream predictors and causes of pregnancy anxiety could improve efforts to identify pregnant women at elevated risk and could eventually lead to reductions in adverse birth outcomes. However, existing theory and research on pregnancy anxiety has not systematically incorporated previous pregnancy experiences. We assessed possible associations between previous pregnancy outcomes and subsequent pregnancy anxiety in the 3D Cohort Study, a Canadian birth cohort. Our objective was to measure the independent contributions of five past pregnancy outcomes (live preterm birth, live birth at term, miscarriage at <20 weeks, stillbirth at ≥20 weeks, and elective abortion) to pregnancy anxiety at three trimesters in a subsequent pregnancy.

Methods: Data on maternal demographic characteristics and pregnancy history for each known previous pregnancy (including those <20 weeks) were collected via interviewer-administered questionnaires at study entry. Pregnancy anxiety for the index study pregnancy was measured prospectively by self-administered questionnaire following each of three prenatal study visits (8 to 14 weeks, 20 to 24 weeks, 32 to 35 weeks).

Results: Of 2366 participants in the 3D Study, 1505 had at least one previous pregnancy. After adjustment for demographic confounding variables and self-reported complications in the index pregnancy, linear regression analyses revealed that prior live term birth was associated with lower pregnancy anxiety at all three trimesters, while prior stillbirth was associated with greater pregnancy anxiety at all three trimesters. Both prior elective abortion and miscarriage were significantly associated with higher pregnancy anxiety scores in the first trimester. Prior preterm birth was associated with

higher pregnancy anxiety in the first trimester in crude analyses, but this association was no longer significant after controlling for confounders.

Discussion: Our study suggests that multiple aspects of obstetric history should be considered along with demographic and psychosocial characteristics as potential predictors of pregnancy anxiety. Our findings can aid in the development of inexpensive screening strategies to identify women at risk of elevated anxiety during pregnancy. Our results can also support research to better target anxiety management interventions in pregnancy and could eventually lead to improvements in birth outcomes.

Introduction

Pregnancy is an area in which prediction and prevention of certain adverse outcomes are troublingly poor [1]. Some, but not all, epidemiologic studies have shown links between psychosocial stress during pregnancy and adverse pregnancy outcomes including preterm birth (PTB) and low birth weight (LBW) [2, 3]. Several conceptual models have been proposed to frame research on stress and birth outcomes. Hogue and colleagues have developed a conceptual framework based on the host-environment-agent triangle of epidemiologic causality [4, 5]. This model posits that exposure to acute and chronic stressors increases the risk of stress-associated pregnancy complications including PTB. However, stress in that model is largely conceptualized in terms not specific to pregnancy, and the role of past pregnancy experiences is not considered in the prediction of stress. Notably, this model does not specifically address pregnancy expectations.

Concerns, fears and worries related to pregnancy that may stem in part from previous pregnancy experiences may be captured by the construct 'pregnancy anxiety' [6]. Some research has identified pregnancy anxiety as a consistent psychosocial predictor of adverse birth outcomes [2, 3, 7-10]. In an investigation of stress and length of gestation in the 3D Cohort Study, we measured the relationships between four forms of psychosocial stress and length of gestation for pregnancies ending in a spontaneous birth [11]. We found that only pregnancy anxiety in the third trimester was significantly associated with shorter gestation after adjustment for maternal education, race, previous PTB, gestational weight gain, and first-trimester vaginal bleeding in the index pregnancy. Though the effect we found on length of gestation in that sample was of a very small magnitude and we found no effect on PTB, work by Dunkel-Schetter and others found pregnancy anxiety to be a more consistent predictor of PTB than other forms of anxiety or psychosocial stress during pregnancy. Stemming from this work, Dunkel-Schetter has developed a conceptual framework that integrates predictors, mediators, and moderating variables to describe how pregnancy anxiety may lead to PTB [2]. Predictors of

pregnancy anxiety incorporated in that model include resilience resources, threat appraisals, anxious predisposition and history of anxiety disorder, medical risks and health communications, and cultural influences on birth and healthcare experiences.

In light of findings on the possible downstream sequelae of pregnancy anxiety, it is important to understand its upstream predictors. This work has potentially important clinical implications in terms of preventing or reducing anxiety during pregnancy. Identifying common predictors of pregnancy anxiety and adverse birth outcomes can also help clarify how strong a causal relationship may exist between the two. Empirically supported predictors of pregnancy anxiety include low maternal age [12, 13], poor physical health [13], low income [12, 14], lack of employment [15], being unmarried [12], dissatisfaction with the marital relationship [15], and other psychological variables including general anxiety [12, 14, 15] and depression [15]. Unintended pregnancy can also be experienced as stressful [16] and has been associated with prenatal anxiety [17] and depressive symptoms [18], as well as postpartum depression [19, 20].

It is noteworthy that in Dunkel-Schetter's model, none of the predictors of pregnancy anxiety is specifically related to previous pregnancy experiences, which could plausibly change pregnancy expectations and affect future pregnancy anxiety. Evidence shows that adverse experiences in pregnancy may alter expectations and increase future anxiety when repeating the pregnancy experience [21, 22]. For example, pregnancy loss (miscarriage or stillbirth) can be experienced as a stressful or traumatic event [23], with symptoms persisting in some cases for 1 to 2 years [24]. Pregnancy loss has also been associated with depression [25, 26], general anxiety [25-27], and pregnancy-specific anxiety [28-31] during a subsequent pregnancy. These effects are not limited to spontaneous pregnancy loss. Elective abortion has also been associated with depression [32, 33], anxiety [32, 33], and psychological distress [34]. Even birth resulting in a healthy child can have negative consequences for maternal mental

health, particularly in the case of emergency Caesarean birth [35-37], PTB [38] or other complications [36, 37, 39, 40].

Empirical evidence supports the inclusion of pregnancy history in a conceptual framework as a determinant of pregnancy anxiety. Pregnancy anxiety has been associated with a prior history of miscarriage [31, 41, 42] or perinatal loss [22, 29, 30, 43], though some studies have failed to find associations between previous adverse pregnancy outcomes and pregnancy anxiety [15, 44]. Studies that included measurements across the pregnancy suggest that prior miscarriage is most strongly associated with anxiety early in a subsequent pregnancy [27, 32, 41, 42]. Further, even in the absence of adverse past pregnancy outcomes, primiparity has also been associated with pregnancy anxiety [13-15, 44]. Consequently, in order to clarify the predictors of pregnancy anxiety and to address some conflicting findings, we propose in a first step to examine the contribution of obstetric history among pregnant women to subsequent pregnancy anxiety in a Canadian cohort. In a second step, our specific objective is to measure in multigravid women the additional independent contributions of five past pregnancy outcomes – live preterm birth, live birth at term, miscarriage at <20 weeks, stillbirth at ≥20 weeks, and elective abortion – to pregnancy anxiety as measured in each of the three trimesters of a subsequent pregnancy. We hypothesized that previous live term births would be significantly associated with lower pregnancy anxiety scores and that previous live preterm births, stillbirths, miscarriages, and elective abortions would be related to higher anxiety scores. Further, we hypothesized that the associations of miscarriage with pregnancy anxiety would be stronger for pregnancy anxiety measured at the beginning of the index pregnancy, whereas the association between stillbirth and pregnancy anxiety would be stronger at the end of the index pregnancy.

Methods

Participants

The 3D Study core cohort comprises 2366 women recruited during the first trimester of pregnancy at one of 10 clinical centres in the province of Québec, Canada. Women were between 18 and 45 years of age at the time of recruitment and fluent in English or French. Exclusion criteria included current illegal drug use, severe illnesses or life threatening conditions, and multiple gestation pregnancies. The sample comprised 42% of 5669 eligible women approached, and 26% of 8974 women approached overall. Of those who participated, 89% completed assessments in French and 11% in English.

Measures

Demographic characteristics examined include maternal age at study entry (<25, 25-29, 30-34, ≥35), total previous pregnancies or gravidity prior to the index pregnancy (none, 1, 2, more than 2), annual household income in Canadian dollars (<30,000, 30,000-49,999, 50,000-99,999, ≥100,000), maternal education level (less than college, college or technical school, university degree, master's or doctoral degree), maternal race (white or other), marital status (married or living with a partner vs. not married/living with a partner), and smoking status (never, former, or current smoker).

Anxiety and depression scales. Pregnancy anxiety was measured using the scale developed by Dunkel-Schetter and colleagues [45]. This scale has been used extensively by this group and others and has been shown to predict adverse birth outcomes including PTB [8]. The instrument pertains to the one-week time period before questionnaire completion and comprises four items scored on a 5-point Likert scale asking participants how often they have felt "anxious", "concerned", "afraid", and "panicky" about being pregnant. The French language version of the pregnancy anxiety scale has been previously validated [8]. Cronbach's α coefficients for the scale ranged from .51 to .72 in previous studies [12, 46-48]. Our observed Cronbach's α coefficients were .84 at all three trimesters. We also administered a 10-

item anxiety disorders screening instrument [49]. Domains covered were: simple phobia, social phobia, panic disorder, agoraphobia, worry, physical anxiety symptoms, obsessions, compulsions, post-traumatic stress, and hypochondria. Each item was rated on a 5-point Likert scale ranging from "never" to "constantly", with the total score calculated as the number of items marked as "sometimes", "often", or "constantly".

Depressive symptoms were measured using the 10-item (first trimester) and 4-item (second and third trimesters) versions of the Center for Epidemiological Studies Depression Scale (CES-D) [50]. The questions are scored on a 4-point Likert scale and pertain to a one-week time period before questionnaire administration. The French version of the CES-D has been previously validated [8]. Cronbach's α coefficients for the scale ranged from .70 to .90 in previous studies [51, 52], while our observed Cronbach's α coefficients ranged from .79 to .82.

Previous pregnancy outcomes. The following previous pregnancy outcomes were examined as exposure variables: live preterm births, live term births, stillbirths at ≥20 weeks, elective abortions, and miscarriages at <20 weeks. We also assessed planned abortion due to fetal anomalies for a secondary analysis. In contrast to other studies that combined early and late pregnancy loss [29, 30, 43], we differentiated miscarriage from stillbirth, enabling a more fine-grained analysis of perinatal loss at different points in the pregnancy.

Procedure

Data on maternal demographic characteristics and pregnancy history for each known previous pregnancy (including those <20 weeks) were collected retrospectively via interviewer-administered questionnaires at study entry. Pregnancy anxiety for the (subsequent) index pregnancy and depressive symptoms were measured by self-administered questionnaire at each of the three prenatal visits (8 to 14 weeks, 20 to 24 weeks, 32 to 35 weeks). The anxiety disorders screening instrument was

administered at the second-trimester assessment. Self-reported complications for the index pregnancy were assessed via interviewer-administered questionnaires at each of the three prenatal study visits.

Statistical analysis

All analyses were carried out using IBM-SPSS for Windows version 21 (IBM Corporation, Armonk, NY, 2012). Missing data were handled using the multiple imputation procedure, with the fully conditional specification algorithm and 5 imputations. This provides estimates of adequate precision given the rates of missing data in our study [53-55]. All exposure variables and covariates were used to create the imputed data sets. We began by examining frequency distributions for all variables included in our analyses. To assure consistency of data, five previous pregnancies with implausible gestational ages were removed. One participant who reported having been pregnant before the index pregnancy but had no data on previous pregnancies was also excluded from our analyses. Because a separate individual questionnaire was filled out for each previous pregnancy and the total number of each previous pregnancy outcome was calculated by counting the occurrences of these forms, there were no implausible values for the counts of previous pregnancy outcomes. Data then met assumptions of statistical tests [56].

We then described the demographic and clinical characteristics of the entire study sample. We examined means and standard deviations for the pregnancy anxiety measure at each of the three trimesters. We compared pregnancy anxiety scores across different strata of the sample using one-way analysis of variance performed with UNIANOVA, which is robust to unbalanced designs. We then examined the distribution of previous pregnancy outcomes, both across the entire sample and within individual participants.

Within the subsample having at least one previous pregnancy, we computed bivariate correlations between previous pregnancy outcomes and subsequent depression and anxiety measures at each of the three trimesters. We used continuous measures identifying the number of times across all

previous pregnancies that a participant had experienced each of the outcomes assessed. For measures showing significant bivariate correlations with the different previous pregnancy outcomes, we tested associations in the multigravid subsample using linear regression models.

In order to avoid developing over-adjusted models and clearly describe any overlapping variance change following the inclusion of potential confounders, we ran crude, partially adjusted, and fully adjusted models for each trimester of the index pregnancy. Each previous pregnancy outcome was considered separately for the crude models, and adjustments were made for all previous pregnancy outcomes in partially adjusted models in order to determine the unique effects of each. For the fully adjusted models we considered other potential confounding variables including demographic and clinical characteristics, self-reported complications in the index pregnancy, depression and anxiety screening score. Smoking was entered categorically, using dummy variables for current smokers and former smokers, with never smokers serving as the reference category.

Results

Study sample and previous pregnancies

The response rates to the self-administered questionnaire were 77% at visit 1, 75% at visit 2 and 70% at visit 3. Response rates were calculated based on all participants who began the study and did not request a complete withdrawal. Thus, participants who did not participate in the 2nd- or 3rd-trimester study visits were still included in the denominator if the outcome of their pregnancy was known. However, response rate calculations for the second and third trimesters excluded participants who had a miscarriage or preterm delivery before the scheduled visit (89 participants at the second-trimester visit, plus a further 41 participants for the third-trimester visit). We conducted sensitivity analyses in which participants who were no longer pregnant at a given study visit were excluded from analyses for previous visits (i.e., the analyses for visit 2 were conducted excluding participants who were no longer

pregnant at visit 3). Results were similar to those for the full data set. Participants reporting Caucasian race, higher household incomes, and higher education levels responded more frequently at all three trimesters, but pregnancy anxiety levels reported at each trimester were not significantly different between participants who were responders vs. non-responders at other trimesters.

Table 1 shows the demographic characteristics of the entire study sample and pregnancy anxiety levels in each trimester during the index pregnancy across strata of those characteristics. Roughly two-thirds of the women were at least 30 years of age at study entry, one-third were primigravida, three-quarters had an annual household income greater than $50,000, about half had a university degree and about one tenth had completed high school or less, 95% were married or living with a partner, two-thirds had never smoked, and 70% self-identified as Caucasian. One-fourth of the participating women reported current pregnancy complications at the first study visit, with fewer reporting complications at the second- and third-trimester visits. Pregnancy anxiety in the first trimester was negatively associated with household income, with a trend towards a negative association in the second trimester as well. Self-reported current pregnancy complications were associated with higher levels of pregnancy anxiety. Pregnancy anxiety at all three trimesters was also significantly higher for non-Caucasian women. Women who were not married or living with a partner reported higher pregnancy anxiety at the first trimester only. Omnibus F-tests of pregnancy anxiety levels by smoking status showed statistically significant differences in the first and second trimesters, while post-hoc comparisons using the Tukey HSD test showed significantly higher pregnancy anxiety among current smokers compared to former smokers in both trimesters ($p = .03$ in first and second trimester). Women with unintended pregnancies reported significantly higher levels of pregnancy anxiety in all three trimesters. The total number of previous pregnancies was not significantly associated with pregnancy anxiety.

Table 2 shows the patterns of previous pregnancies and previous pregnancy outcomes across the 1505 multigravid participants. Of 2912 total previous pregnancies, roughly half resulted in a live birth, one quarter in miscarriage and one fifth in elective abortion. 70% of participants had at least one live birth, 37% at least one previous miscarriage, 28% at least one elective abortion, and 3% at least one prior stillbirth.

Correlations between previous pregnancy outcomes and index pregnancy anxiety, depressive symptoms and anxiety disorder screening scores

Table 3 shows bivariate correlations between previous pregnancy outcomes and index pregnancy anxiety, depressive symptoms and anxiety disorder screening scores among the subsample of 1505 multigravid participants. The number of previous live term births was significantly correlated with lower pregnancy anxiety in all three trimesters. Prior stillbirth and elective abortion were both associated with higher pregnancy anxiety in all three trimesters. We observed significant positive correlations between both prior miscarriage and prior PTB with pregnancy anxiety in the first trimester of the index pregnancy. None of the previous pregnancy outcomes displayed strong relationships with depressive symptoms or anxiety disorder screening score in the index pregnancy.

Multivariate analyses

Data were missing more frequently for participants with lower household incomes or education levels and from racial minorities. The overall response rates were 59% and 60% for participants in the lowest household income and education categories respectively, whereas they were 80% in the highest categories. Response rates were 78% for participants identifying as white and 62% for non-white participants.

Table 4 shows the results of multivariate linear regression analyses examining the associations of previous pregnancy outcomes among multigravid participants with index pregnancy anxiety in each trimester. The crude models show the unadjusted parameters for each past pregnancy outcome. The

partially adjusted analyses show that prior live term birth, stillbirth and elective abortion were each independently associated with pregnancy anxiety in all three trimesters of the index pregnancy and contribute together about 4% of the variance in predicting first-trimester pregnancy anxiety, a percentage that dropped gradually to slightly less than 2% in the third trimester. Adjustment for covariates increased the percent of variance accounted for by the models to 9% in the first trimester, down to 6% in the third trimester. Among covariates, predictors of pregnancy anxiety included unintended pregnancy, self-reported complications, smoking status and non-white race, though these covariates were not consistently significant across trimesters. Associations for live term birth and elective abortion were opposite in direction but of similar magnitude before and after adjusting for other previous pregnancy outcomes and covariates. The association between prior stillbirth and pregnancy anxiety maintained statistical significance in adjusted analyses in the third trimester. The magnitude of associations was generally in the low range (absolute value of B for significant associations ranging from 0.11 to 0.13) but was of moderate size for stillbirth (B = 0.40, 95% CI = 0.05, 0.74 in the third trimester). Additionally, the pattern of associations for live term births, stillbirths and elective abortions exhibited considerable homogeneity across the three trimesters in adjusted analyses. Prior miscarriage was significantly associated with pregnancy anxiety only in the first trimester of the index pregnancy. Overall, live births, stillbirths and elective abortions were associated with pregnancy anxiety across trimesters, and miscarriages were associated with pregnancy anxiety in the first trimester in adjusted analyses.

In an attempt to determine whether pregnancy anxiety in the index pregnancy was related to the reason for a previous elective abortion, we conducted a follow-up sensitivity analysis in which we separated planned abortions due to fetal anomalies from other elective abortions. Associations for planned abortions due to fetal anomalies were several times stronger than those for other elective abortions and were statistically significant in the second trimester (Table 5).

Alternative modeling strategies

Our principal analyses were conducted using linear regression models, with missing data imputed using multiple imputation. In order to test some of the underlying psychometric assumptions in these models, we also ran our main analyses using a structural equation modeling technique [57], with missing data handled using full-information maximum likelihood [58]. For this analysis, factor scores were constructed for the pregnancy anxiety measure at each time point. Factor loadings from principal components analysis were consistently high (>.6) for each of the four items in the pregnancy anxiety scale. The final structural equation model included regression paths from each of the prior pregnancy outcome variables to the latent pregnancy anxiety variables at each time point. Coefficients were of similar magnitude and in the same direction as those from the linear regression models reported earlier. We therefore chose to use the simpler linear regression models.

Discussion

In our initial analysis on the entire 3D cohort, we did not find significant associations between the number of previous pregnancies and pregnancy anxiety in the index pregnancy. We then examined, in the subsample of multigravid women, whether five previous pregnancy outcomes predicted pregnancy anxiety in a subsequent pregnancy over and above several potential confounders. Prior live term birth was significantly related to lower pregnancy anxiety, while prior stillbirths, miscarriages, and elective abortions were significantly associated with greater pregnancy anxiety. The associations for live term births, stillbirths and elective abortions were observed in all three trimesters of pregnancy, while the association for miscarriage was stronger and statistically significant only for first-trimester pregnancy anxiety. These findings were largely robust to adjustment for demographic and socioeconomic variables and were consistently in the directions we hypothesized. Among the confounding variables, and as expected, maternal race, unintended pregnancy and concurrent self-

reported pregnancy complications exhibited bivariate associations with pregnancy anxiety across the three trimesters in the entire cohort. These associations largely persisted in the final models with adjustment for previous pregnancy outcomes. Our finding that prior PTB was associated in crude analyses with pregnancy anxiety only in the first trimester was unexpected, while the findings for prior miscarriages and stillbirths were in line with our hypotheses regarding when in the pregnancy these exposures would exhibit the strongest effects.

Total previous pregnancies and live births

The relationship reported here between previous live term births and lower pregnancy anxiety corroborates results reported from Saisto et al. [15] (standardized B = -0.15; 95% CI = -0.28, -0.02). The magnitude of the association reported in that study was similar to those observed in our cohort: standardized B ranging from -0.13 to -0.16. One potential explanation for this association is that it may be driven by the experience of previous pregnancy and successful childbirth. However, Saisto et al. point out that fears of pregnancy and childbirth may be related to more generalized anxiety, life dissatisfaction, and difficulty coping with demanding life events for newly expectant mothers. It is also plausible that women in that study who have had more previous live births would later be coping with greater family demands and stresses. Therefore, whatever anxiety these women experience may be more focused on such pre-existing demands than on a new pregnancy. If this is so, however, such anxiety was not captured by the additional measures we examined, as prior live term births were not associated with depression or symptoms of anxiety disorders.

Miscarriage at <20 weeks

As expected, we found evidence for an association between prior miscarriage at <20 weeks and pregnancy anxiety in early pregnancy, with no association at mid- or late pregnancy in adjusted analyses. This finding is consistent with several studies that have found elevated pregnancy anxiety scores among participants with a history of miscarriage [31, 41, 42], with stronger effects earlier in

pregnancy [42] and dose-response effects for the number of previous miscarriages [31]. Our findings for prior miscarriage contrast with those of two studies that found no association between history of miscarriage and pregnancy-specific distress or pregnancy anxiety [15, 44]. In a study on psychosocial predictors of pregnancy anxiety and fear of vaginal childbirth, Saisto et al. looked in an exploratory capacity at previous pregnancy outcomes [15]. They found no significant correlation between previous spontaneous or induced abortions and pregnancy anxiety and did not further examine these variables in multivariate analyses. The pregnancy anxiety scale used in Saisto's study measured anxiety about being pregnant, childbirth, and hospitalization [59], and thus included a broader range of domains than was measured in our study. Saisto et al. measured pregnancy anxiety at one time point for each participant in the study, and the timing of measurement varied across all three trimesters in the study sample. Another study [44] on the relationship between previous pregnancy experiences and maternal distress in pregnancy found no significant associations between prior miscarriage and pregnancy-specific distress as measured in each of the three trimesters by a revised version of the Prenatal Distress Questionnaire (PDQ) [60]. That instrument measures the extent to which a woman is distressed by changes resulting from the pregnancy such as physical symptoms, paying for medical care, and changes in relationships. This stands in contrast to our pregnancy anxiety measure, which focuses on women's concerns about the course and outcome of the pregnancy. The use of these different scales may be responsible for the differences in findings between our study and others.

Stillbirth at ≥20 weeks

As expected, we observed a positive association between prior stillbirth at ≥20 weeks and pregnancy anxiety that was strongest and statistically significant in the third trimester, between 32 and 35 weeks. Our findings are similar to that of Armstrong and Hutti [22], who found that women with a history of perinatal loss (late pregnancy miscarriage, stillbirth or neonatal death) had higher pregnancy

anxiety scores at mid to late pregnancy, though that study measured pregnancy anxiety cross-sectionally only at one time point.

Elective abortion

We found an association between prior elective abortion and pregnancy anxiety that was strongest in the first trimester. The association was largely robust to adjustment for other previous pregnancy outcomes, demographic characteristics and self-reported pregnancy complications, with effects of borderline significance observed in second- and third-trimester adjusted analyses. We also found stronger associations for planned elective abortion due to fetal anomalies. It is plausible that this finding stems from patients' concerns over the possible recurrence of fetal anomalies.

Very few studies have explored the relationship between prior elective abortions and pregnancy anxiety. Our findings are consistent with previous studies linking a history of elective abortion with general anxiety [32, 33] and psychosocial stress [34] in a subsequent pregnancy, but are inconsistent with the study by Saisto et al. [15], who found no association between prior elective abortion and either pregnancy anxiety or fear of vaginal childbirth. However, that study had a smaller sample size (N=278) and was not designed specifically to look at previous pregnancy outcomes.

Systematic reviews have found associations between elective abortion and subsequent PTB [61, 62] and LBW [61]. Combined with our results linking elective abortion to subsequent pregnancy anxiety, these findings support the need to improve evidence-based communication with pregnant women who have previously had an abortion about how to minimize the risks to their current pregnancy. A trial examining social support for pregnant women with a history of elective abortion could shed light on whether this type of intervention has the potential to reduce anxiety or to improve pregnancy outcomes in this population. However, it remains to be determined what types of social support could be the most effective, as well as the best source of social support.

Demographic characteristics

Lynn et al. suggest that pregnancy anxiety, in contrast to other types of stress, may be experienced irrespective of social status [13]. Pregnancy anxiety displayed some correlations with adversity indices such as income, maternal age, smoking and family status in our study population, but these links were not consistent across the pregnancy. Our findings of stronger associations between these characteristics and anxiety early in pregnancy adds to the findings of Lynn et al., who assessed pregnancy-related stress at only one time point in the second or third trimester.

Psychological mechanisms and clinical implications

Women who have experienced perinatal loss or other adverse pregnancy outcomes in the past may become conditioned to fear a repetition of these outcomes in future pregnancies [21, 22, 29, 31, 41, 43]. In assessing the psychological component of pregnancy anxiety rather than using a somatic or biological measurement, our study specifically focused on such concerns. Our measurement of pregnancy anxiety at multiple time points also permitted us to test how such apprehension was tied to the timing of the adverse event from the former pregnancy.

The brevity and demonstrated psychometric properties of the pregnancy anxiety measure suggest that screening for pregnancy anxiety could be carried out quickly and inexpensively. The results of our study could be used to inform the process of creating a predictive model to identify high-risk women for pregnancy anxiety screening. Our findings suggest that multiple aspects of obstetric history need to be considered along with demographic and psychosocial characteristics as potential predictors of pregnancy anxiety.

Limitations

Response rates to the self-administered questionnaires from which our outcome variables were taken ranged from 70% to 77%. Non-responders tended to be lower-SES, higher-risk participants and also had slightly higher pregnancy anxiety scores at other time points. A small amount of data were

missing for covariates as well. We imputed missing data in an attempt to reduce any resulting bias. The multiple imputation algorithm provides more accurate estimates of precision than single imputation [54], but the validity of the procedure rests on the assumption that data are missing at random [55], which may not be the case in our study, as missingness was associated with some demographic characteristics that were themselves associated with the outcome variables. If data were more frequently missing for those higher-risk participants who also had higher pregnancy anxiety scores, our results would be biased towards the null hypothesis even after imputing missing values.

We also recognize that self-reported pregnancy history may be subject to recall bias and will underestimate the true incidence of miscarriage, as some pregnancies ending in miscarriage go unrecognized [63]. Our study investigated the posited psychological sequelae of previous pregnancy experiences as known and understood by the woman, not the biological risk factors that may have led to previous unrecognized miscarriages and which could presumably affect the course of future pregnancies. Therefore, only miscarriages that were recognized would be relevant to our study. However, it is plausible that women who are more anxiety-prone would be more apt to recognize and report "borderline" previous miscarriages (i.e., alterations in the menstrual cycle that may or may not have been true miscarriages), which would lead to an artificial inflation of our findings. We note that 277 women in the 3D cohort (11.7%) became pregnant with the use of ovulation-inducing drugs or other assisted reproductive technologies. It is likely that the use of such technologies or underlying infertility is related to anxiety and other aspects of mental health during pregnancy [64, 65]. In light of wide heterogeneity in the types of assisted reproductive technologies used, exploration of their effects on pregnancy anxiety falls outside the scope of the present study.

We also did not measure the timing of previous miscarriages or elective abortions. In one study examining the timing of the miscarriage as a possible moderator of its effects on maternal mental health in a subsequent pregnancy, state anxiety scores were found to be significantly higher among

participants who had not yet passed the corresponding point in their current pregnancy when a miscarriage had occurred in a previous pregnancy, with no difference found for pregnancy anxiety [31]. Our observed relationship between pregnancy complications and pregnancy anxiety is difficult to compare with existing literature, as studies have tended to define medical risk as a combination of medical history and current pregnancy complications [12, 46, 47], while a major focus of our study was to separate these two. Finally, while we differentiated previous miscarriage from stillbirth, we did not collect data on neonatal death following previous pregnancies. This gave us a narrower definition of perinatal loss than studies that included postnatal loss [29, 30, 43].

Our decision to adjust for self-reported pregnancy complications may be questioned, as this variable could lie on the causal path between our exposures and outcome. Presentation of the adjusted results in effect shows the direct association between previous pregnancy outcomes and pregnancy anxiety, removing any indirect effect through complications in the index pregnancy. While complications were a strong predictor of pregnancy anxiety, excluding this variable from the final models did not substantially change the estimates for the principal exposure variables.

Conclusions

This study examined several previous pregnancy outcomes to add to the literature on the relationship between obstetric history and anxiety in future pregnancies. Our principal findings regarding correlates of pregnancy anxiety are plausible and are largely in line with existing literature. However, much of this literature has combined different adverse pregnancy outcomes and has looked at pregnancy anxiety only at one or two prenatal time points. Our study thus extends on the previous literature by examining the independent contributions of several previous pregnancy outcomes to subsequent pregnancy anxiety in three trimesters, enabling a more refined view of how obstetric history

is related to maternal anxiety across a subsequent pregnancy. Our findings can support research to improve the targeting of anxiety management interventions in pregnancy.

Pregnancy anxiety may be at least in part a non-causal marker of heightened risk for adverse birth outcomes [5]. Previous studies exploring associations between pregnancy anxiety and subsequent birth or childhood outcomes have generally controlled for obstetric or medical risk as a dichotomous [7, 66] or continuous [46, 47, 67-70] variable. Our results showing independent links between several aspects of obstetric history and pregnancy anxiety suggest that the patient's entire obstetric history needs to be considered in addressing concerns about the current pregnancy. Evidence-based intervention programmes are likely to be more effective if they take into effect the full range of the patient's obstetric experience, including prior pregnancy outcomes. From a theoretical and research perspective, our study shows that framing obstetric risk as a multidimensional concept as opposed to a single score may help elucidate the extent to which anxiety concerning a current pregnancy finds its origins in specific and independent previous pregnancy experiences.

Table 1. Sample characteristics and pregnancy anxiety, entire 3D sample, N = 2365

		N (%)		Pregnancy anxiety: mean (std. dev.)		
				1st trimester	2nd trimester	3rd trimester
Overall		2365	(100%)	3.69 (3.29)	3.13 (2.98)	3.29 (2.94)
Maternal age	<25	173	(7%)	4.13 (3.44)	3.02 (3.00)	3.25 (2.71)
	25-29	751	(32%)	3.65 (3.30)	3.21 (3.01)	3.34 (2.88)
	30-34	917	(39%)	3.50 (3.15)	3.03 (2.76)	3.27 (2.96)
	≥35	519	(22%)	3.99 (3.47)	3.27 (3.32)	3.28 (3.07)
	Comparison			*F(3, 1805) = 2.50, p = .06, eta² = 0.004*	*F(3, 1692) = 0.68, p = .56, eta² = 0.001*	*F(3, 1566) = 0.07, p = .98, eta² = 0.000*
Previous pregnancies	0	860	(36%)	3.77 (3.09)	3.30 (2.86)	3.51 (2.86)
	1	761	(32%)	3.43 (3.29)	2.93 (2.81)	3.19 (2.91)
	2	380	(16%)	3.72 (3.53)	2.97 (2.96)	3.05 (2.87)
	>2	364	(15%)	3.99 (3.51)	3.28 (3.63)	3.14 (3.26)
	Comparison			*F(3, 1807) = 2.10, p = .10, eta² = 0.003*	*F(3, 1696) = 1.96, p = .12, eta² = 0.003*	*F(3, 1569) = 2.04, p = .11, eta² = 0.004*
Household income	<30,000	256	(11%)	4.54 (3.93)	3.64 (3.40)	3.56 (3.33)
	30,000-49,999	286	(13%)	3.98 (3.46)	3.40 (3.28)	3.32 (3.04)
	50,000-99,999	1017	(45%)	3.67 (3.24)	3.10 (2.88)	3.34 (2.93)
	≥100,000	688	(31%)	3.41 (3.03)	2.96 (2.83)	3.10 (2.73)
	Comparison			*F(3, 1726) = 5.47, p < .01, eta² = 0.009*	*F(3, 1632) = 2.58, p = .05, eta² = 0.005*	*F(3, 1502) = 1.17, p = .32, eta² = 0.002*
Maternal education	Less than college	254	(11%)	3.96 (3.58)	3.16 (2.94)	3.15 (2.93)
	College or technical school	619	(27%)	3.90 (3.57)	3.22 (3.29)	3.45 (3.20)
	University degree	911	(39%)	3.62 (3.12)	3.22 (2.94)	3.35 (2.84)
	Master's or doctoral degree	532	(23%)	3.47 (3.10)	2.82 (2.67)	3.07 (2.83)
	Comparison			*F(3, 1772) = 1.74, p = .16, eta² = 0.003*	*F(3, 1663) = 1.89, p = .13, eta² = 0.003*	*F(3, 1543) = 1.28, p = .28, eta² = 0.002*
Maternal race	White	1636	(69%)	3.53 (3.15)	2.92 (2.79)	3.14 (2.80)
	Other	722	(31%)	4.16 (3.63)	3.76 (3.42)	3.71 (3.28)
	Comparison			*F(1, 1806) = 12.84, p < .01, eta² = 0.007*	*F(1, 1695) = 26.45, p < .01, eta² = 0.015*	*F(1, 1568) = 11.26, p < .01, eta² = 0.007*

		N (%)		Pregnancy anxiety: mean (std. dev.)		
				1st trimester	2nd trimester	3rd trimester
Marital status	Married or living with a partner	2232	(95%)	3.62 (3.24)	3.12 (2.97)	3.30 (2.94)
	Not married or living with a partner	127	(5%)	5.01 (3.96)	3.39 (3.37)	3.01 (2.98)
	Comparison			*F(1, 1807) = 14.52, p < .01, eta² = 0.008*	*F(1, 1695) = 0.55, p = .46, eta² = 0.000*	*F(1, 1569) = 0.63, p = .43, eta² = 0.000*
Smoking	Never	1331	(65%)	3.72 (3.29)	3.11 (2.93)	3.37 (3.01)
	Former	408	(20%)	3.31 (3.20)	2.92 (2.82)	3.00 (2.89)
	Current	303	(15%)	4.04 (3.34)	3.59 (3.15)	3.42 (2.88)
	Comparison			*F(2, 1561) = 3.43, p = .03, eta² = 0.004*	*F(2, 1485) = 3.30, p = .04, eta² = 0.004*	*F(2, 1370) = 1.93, p = .15, eta² = 0.003*
Intended pregnancy	Yes	1583	(91%)	3.50 (3.13)	3.05 (2.90)	3.20 (2.84)
	No	150	(9%)	5.27 (3.96)	4.16 (3.58)	4.55 (3.79)
	Comparison			*F(1, 1316) = 27.19, p < .01, eta² = 0.020*	*F(1, 1233) = 10.17, p < .01, eta² = 0.008*	*F(1, 1155) = 15.31, p < .01, eta² = 0.013*
Self-reported complications first trimester	Yes	578	(24%)	4.21 (3.50)	3.74 (3.39)	3.42 (2.86)
	No	1787	(76%)	3.52 (3.21)	2.95 (2.82)	3.25 (2.96)
	Comparison			*F(1, 1809) = 14.31, p < .01, eta² = 0.008*	*F(1, 1698) = 21.66, p < .01, eta² = 0.013*	*F(1, 1571) = 0.99, p = .32, eta² = 0.001*
Self-reported complications second trimester	Yes	267	(13%)	4.26 (3.76)	4.23 (3.69)	3.78 (3.26)
	No	1863	(87%)	3.56 (3.20)	2.98 (2.84)	3.19 (2.85)
	Comparison			*F(1, 1718) = 8.52, p < .01, eta² = 0.005*	*F(1, 1688) = 31.72, p < .01, eta² = 0.018*	*F(1, 1548) = 6.80, p = .01, eta² = 0.004*
Self-reported complications third trimester	Yes	320	(16%)	3.64 (3.52)	3.20 (3.07)	3.71 (3.04)
	No	1722	(84%)	3.67 (3.24)	3.12 (2.95)	3.22 (2.92)
	Comparison			*F(1, 1648) = 0.02, p = .88, eta² = 0.000*	*F(1, 1646) = 0.18, p = .67, eta² = 0.000*	*F(1, 1567) = 5.82, p = .02, eta² = 0.004*

Table 2. Previous pregnancy outcomes, multigravid participants subsample, N = 1505, reporting 2912 pregnancies

Pregnancy outcome	Total pregnancies[a]	Percentage of all pregnancies	Participants with at least one outcome	Percent of all participants[b]	Maximum number of outcomes per participant
Live preterm singleton birth	148	5.1%	143	9.5%	5
Live term singleton birth	1275	43.9%	955	63.5%	10
Live multiple births	16	0.6%	16	1.1%	1
Stillbirth, >20weeks	49	1.7%	47	3.1%	2
Live birth(s) and stillbirth of (an)other twin(s)	4	0.1%	4	0.3%	1
Elective abortion	548	18.9%	423	28.1%	5
Miscarriage, <20weeks	799	27.5%	546	36.3%	9
Molar pregnancy	12	0.4%	11	0.7%	2
Ectopic pregnancy	43	1.5%	37	2.5%	3

[a]Pregnancy outcome data missing for 18 previous pregnancies

[b]Percentages within the column add up to more than 100% as some participants experienced a given previous pregnancy outcome more than once.

Table 3. Correlations between major study variables, multigravid participants subsample, maximum N = 1505

	N	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.
1. Maternal age	1503	-														
2. Household income	1432	.19**	-													
3. Maternal education	1479	.30**	.35**	-												
4. Number of previous pregnancies	1505	.19**	-.12**	-.12**	-											
5. Number of previous live preterm births	1505	.10**	-.01	-.02	.18**	-										
6. Number of previous live term births	1505	.14**	-.08**	-.06*	.47**	-.14**	-									
7. Number of previous stillbirths	1505	.02	-.02	-.10**	.14**	.07**	-.01	-								
8. Number of previous elective abortions	1505	-.08**	-.07**	-.10**	.32**	-.04	-.18**	-.06*	-							
9. Number of previous miscarriages	1505	.14**	-.02	-.01	.64**	.02	.00	.04	-.09**	-						
10. Pregnancy anxiety 1st trimester	1114	.03	-.13**	-.07*	.06*	.06*	-.12**	.08**	.11**	.09**	-					
11. Pregnancy anxiety 2nd trimester	1026	.05	-.09**	-.05	.05	.02	-.10**	.09**	.11**	.05	.60**	-				
12. Pregnancy anxiety 3rd trimester	963	.00	-.09**	-.02	.00	.01	-.09**	.09**	.08*	-.01	.52**	.61**	-			
13. Depression 1st trimester	1114	-.02	-.18**	-.07*	.04	.03	.00	.01	.05	.02	.50**	.33**	.35**	-		
14. Depression 2nd trimester	1022	-.08**	-.20**	-.12**	.04	.01	.02	.04	.04	.00	.30**	.38**	.30**	.51**	-	
15. Depression 3rd trimester	965	.04	-.16**	-.01	.10**	.07*	.06*	.04	.02	.02	.28**	.29**	.42**	.41**	.48**	-
16. Anxiety disorders screening scale 2nd trimester	1025	-.07*	-.15**	-.14**	.05	.04	-.05	.05	.05	.05	.33**	.32**	.31**	.38**	.38**	.28**

* p < .05, ** p < .01

Table 4. Results of multiple linear regression analyses between previous pregnancy outcomes and subsequent pregnancy anxiety at each trimester, multigravid participants subsample, N = 1505

	Crude models			Partially adjusted models *		Fully adjusted models *	
	B (95% CI)	**p**	**R^2**	**B (95% CI)**	**p**	**B (95% CI)**	**p**
1st trimester							
Live preterm births	**0.23 (0.03, 0.44)**	**.03**	.007	0.19 (-0.01, 0.39)	.06	0.16 (-0.04, 0.36)	.10
Live term births	**-0.14 (-0.23, -0.06)**	**<.01**	.015	**-0.11 (-0.19, -0.03)**	**.01**	**-0.13 (-0.21, -0.05)**	**<.01**
Stillbirths	**0.38 (0.01, 0.74)**	**.04**	.006	0.36 (0.01, 0.71)	.05	0.30 (-0.10, 0.70)	.13
Elective abortions	**0.16 (0.05, 0.28)**	**.01**	.012	**0.16 (0.05, 0.27)**	**.01**	**0.13 (0.03, 0.24)**	**.01**
Miscarriages	**0.11 (0.04, 0.18)**	**<.01**	.009	**0.12 (0.05, 0.19)**	**<.01**	**0.11 (0.03, 0.18)**	**.01**
Income						-0.02 (-0.05, 0.02)	.37
Non-white race						0.13 (-0.01, 0.27)	.06
Current smoker						0.06 (-0.21, 0.32)	.64
Former smoker						**-0.23 (-0.39, -0.06)**	**.01**
Unintended pregnancy						**0.51 (0.31, 0.71)**	**<.01**
Self-reported complications						**0.21 (0.09, 0.33)**	**<.01**
				$F(5,1499) = 13.85$, $p < .01$, $R^2 = 0.04$		$F(11,1493) = 15.09$, $p < .01$, $R^2 = .09$	
2nd trimester							
Live preterm births	0.09 (-0.15, 0.32)	.45	.001	0.05 (-0.18, 0.27)	.66	0.00 (-0.21, 0.21)	.99
Live term births	**-0.13 (-0.20, -0.06)**	**<.01**	.013	**-0.11 (-0.18, -0.04)**	**<.01**	**-0.13 (-0.20, -0.05)**	**<.01**
Stillbirths	**0.37 (0.06, 0.68)**	**.02**	.008	**0.38 (0.07, 0.69)**	**.02**	0.24 (-0.08, 0.57)	.14
Elective abortions	**0.14 (0.03, 0.25)**	**.01**	.007	**0.13 (0.02, 0.24)**	**.02**	0.11 (0.00, 0.21)	.05
Miscarriages	0.05 (-0.02, 0.11)	.17	.002	0.05 (-0.01, 0.12)	.11	0.04 (-0.02, 0.10)	.19
Income						-0.01 (-0.05, 0.04)	.78
Non-white race						**0.17 (0.09, 0.26)**	**<.01**
Current smoker						0.13 (-0.07, 0.32)	.20
Former smoker						-0.13 (-0.31, 0.06)	.17
Unintended pregnancy						**0.51 (0.32, 0.70)**	**<.01**
Self-reported complications						**0.38 (0.19, 0.56)**	**<.01**
				$F(5,1441) = 7.60$, $p < .01$, $R^2 = .02$		$F(11,1435) = 13.52$, $p < .01$, $R^2 = .09$	

	Crude models			Partially adjusted models *		Fully adjusted models *	
	B (95% CI)	**p**	**R^2**	**B (95% CI)**	**p**	**B (95% CI)**	**p**
3rd trimester							
Live preterm births	0.05 (-0.13, 0.22)	0.60	<.001	0.01 (-0.16, 0.18)	.95	-0.04 (-0.22, 0.13)	.64
Live term births	**-0.11 (-0.19, -0.03)**	**0.01**	.008	**-0.09 (-0.17, -0.01)**	**.02**	**-0.13 (-0.20, -0.06)**	**<.01**
Stillbirths	**0.43 (0.12, 0.74)**	**0.01**	.007	**0.45 (0.14, 0.75)**	**<.01**	**0.40 (0.05, 0.74)**	**.02**
Elective abortions	**0.13 (0.03, 0.22)**	**0.01**	.006	**0.11 (0.01, 0.21)**	**.03**	0.09 (0.00, 0.18)	.06
Miscarriages	-0.02 (-0.09, 0.05)	0.51	<.001	-0.02 (-0.09, 0.05)	.60	-0.02 (-0.09, 0.06)	.64
Income						0.01 (-0.03, 0.05)	.50
Non-white race						**0.12 (0.01, 0.22)**	**.03**
Unintended pregnancy						**0.59 (0.21, 0.96)**	**.01**
Self-reported complications						**0.22 (0.03, 0.41)**	**.02**
				$F(5,1410) = 5.85$, $p < .01$, $R^2 = .02$		$F(9,1406) = 11.12$, $p < .01$, $R^2 = .06$	

* Partially adjusted models include adjustment for each previous pregnancy outcome; fully adjusted models include adjustment for other listed variables as well.

Table 5. Results of multiple linear regression analyses between prior elective abortion for fetal anomalies, other prior elective abortion and subsequent pregnancy anxiety, multigravid participants subsample, N = 1505

		Crude models			Adjusted models[a]	
	n[b]	**B (95% CI)**	**p**		**B (95% CI)**	**p**
1st trimester						
Abortion for fetal anomalies	28	**0.60 (0.23, 0.97)**	**<.01**	$F(1,1503) = 11.12$, $p < .01$, $R^2 = .007$	0.13 (-0.01, 0.27)	0.06
Abortion not for fetal anomalies	397	**0.14 (0.02, 0.26)**	**.03**	$F(1,1503) = 13.46$, $p < .01$, $R^2 = .008$	0.05 (-0.21, 0.32)	0.66
					$F(11,1493) = 14.35$, $p < .010$, $R^2 = .09$	
2nd trimester						
Abortion for fetal anomalies	27	**0.65 (0.29, 1.02)**	**<.01**	$F(1,1445) = 12.67$, $p < .01$, $R^2 = 0.008$	**0.73 (0.37, 1.08)**	**<.01**
Abortion not for fetal anomalies	378	**0.11 (0.00, 0.22)**	**.05**	$F(1,1445) = 8.49$, $p = 0.02$, $R^2 = 0.005$	0.06 (-0.04, 0.16)	.23
					$F(11,1337) = 13.07$ $p < .01$, $R^2 = .09$	
3rd trimester						
Abortion for fetal anomalies	26	0.16 (-0.21, 0.53)	0.41	$F(1,1414) = 0.70$, $p = .41$, $R^2 < .001$	0.19 (-0.17, 0.55)	.30
Abortion not for fetal anomalies	368	**0.12 (0.03, 0.22)**	**0.01**	$F(1,1414) = 9.47$, $p < .01$, $R^2 = .006$	0.07 (-0.04, 0.18)	.21
					$F(9,1271) = 9.55$, $p < .01$, $R^2 = .06$	

[a]Adjusted for other previous pregnancy outcomes and other confounding variables from Table 4

[b]Number of women with at least one outcome

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Information sur l'article

Chapitre 5 : Previous Pregnancy Outcomes and Subsequent Pregnancy Anxiety in the 3D Cohort Study

Titre de l'article : Previous Pregnancy Outcomes and Subsequent Pregnancy Anxiety: The 3D Cohort Study

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Chapitre 6

Conclusions et directions futures

Résumé et défis futurs

Cette thèse s'est concentrée sur deux grands enjeux principaux de la santé mentale périnatale : la dépression postnatale (DPN) et le stress psychosocial pendant la grossesse (SPG). Ces deux problèmes ont des impacts sur la santé maternelle, mais peuvent aussi affecter de façon importante la santé et le développement de l'enfant. Les effets de la DPN sur l'enfant sont médiés par des facteurs relationnels entre la mère et l'enfant, alors que pour le stress psychosocial pendant la grossesse, les effets sont souvent médiés par les issues de la grossesse. Dans tous les cas, les troubles maternels de santé mentale peuvent laisser des séquelles à long terme dans la vie de l'enfant.

Défis pour la dépression postnatale

Des avances prometteuses ont été faites sur le plan de la prévention [185, 186] et du traitement [187-192] de la DPN. Une connaissance de plus en plus approfondie est également utile pour contrer la stigmatisation de la DPN [193] et les effets de celle-ci comme barrière au traitement [194-196]. Néanmoins, il reste des lacunes dans la compréhension de la neurobiologie sous-jacente [197]. Des chercheurs ont proposé de considérer la dépression périnatale comme un syndrome distinct des autres dépressions sur le plan neurologique [198], mais les différences entre la dépression périnatale et celle qui survient à d'autres moments de la vie demeurent mal comprises [199]. Si finalement de telles différences biologiques sont révélées, cela suggérerait une orientation de recherche spécifiquement axée sur le profil de la dépression périnatale. Si par contre les différences trouvées restent davantage sur le plan social (par exemple, expériences subjectives, vulnérabilité intensifiée à des facteurs de risque

sociaux), cela impliquerait plutôt de mettre l'accent sur les défis maternels et la recherche de thérapies qui tiennent compte des besoins et des ressources sociales de cette population.

Les facteurs de risque génétiques et nutritionnels pour la dépression postnatale. Plusieurs études discutent d'une composante génétique de la vulnérabilité à la dépression [200], y compris à la DPN [201-203]. La possibilité qu'il existe un lien entre la dépression et le génotype du transporteur de sérotonine reste un champ prometteur dans ce domaine [204, 205], mais un tel lien n'est pas encore définitivement établi. Les avancées concernant la compréhension des composantes génétiques peuvent mener à des améliorations dans le dépistage, le conseil génétique et le développement de nouvelles interventions biologiques.

Un corpus de littérature toujours croissant se penche sur les composantes nutritionnelles de la DPN [206-209], particulièrement sur les acides gras oméga-3 (n-3 PUFA) [155, 158, 210-212]. Ces recherches sont importantes afin de mieux comprendre l'aspect neurologique de la dépression et comment cette dernière peut être affectée par des changements hormonaux lors de la période périnatale [213]. De plus, l'apport nutritionnel est un facteur de risque potentiellement modifiable. Comme il est décrit dans le chapitre 2, l'apport d'acides gras oméga-3 est fortement insuffisant chez les femmes enceintes. En plus, les n-3 PUFA sont associés à des effets positifs sur la grossesse et sur la santé et le développement de l'enfant [214].

La possibilité d'une interaction entre le génotype 5-HTT et les n-3 PUFA dans le développement de la DPN demeure une hypothèse pour laquelle les appuis ne sont pas encore assez suffisantes pour faire autorité. Néanmoins, l'exploration de cette hypothèse constitue un des volets parmi les diverses techniques utilisées afin d'accroître la compréhension de la DPN ainsi que sa prévention et son traitement.

Défis pour la naissance prématurée

La naissance prématurée (NP) s'avère actuellement l'un des problèmes principaux de l'obstétrique [91]. Cette problématique a démontré une hétérogénéité [215, 216] et une complexité biologique [217] qui rendent difficiles les efforts de prédiction et de prévention [218, 219]. Le taux de NP n'a pas manifesté la même décroissance que d'autres problèmes de santé néonatale [220-222], mais plutôt une augmentation dans plusieurs pays [88, 223]. Les disparités entre des différentes populations concernant les taux de prématurité sont aussi troublantes [224, 225].

Stress psychosocial pendant la grossesse et prématurité. Le chapitre 3 a évoqué plusieurs voies émergentes destinées à la recherche sur les liens entre le stress pendant la grossesse et la prématurité. L'examen des biomarqueurs du stress peut venir enrichir les résultats de notre examen des mesures psychosociales du stress. Notamment, la caractérisation du microbiome vaginal en relation avec le niveau de stress maternel et le *monitoring* non-invasif de l'activité cholinergique présentent des possibilités prometteuses dans la prédiction de l'accouchement prématuré, et ce, avec plus d'efficacité que les outils actuellement disponibles. Depuis la publication de l'article du chapitre 3 [226], des progrès plus poussés ont été achevés dans ces domaines [227, 228]. À la suite de notre discussion de la variabilité de fréquence cardiaque (VFC) et de sa relation avec le stress pendant la grossesse, une étude d'intervention également intéressante du *biofeedback* de la VFC chez les patientes ayant un travail prématuré a présenté des évaluations réduites du stress chronique dans le groupe d'intervention [229].

Études futures en santé mentale périnatale

Cette thèse a exploré plusieurs hypothèses concernant les antécédents et séquelles des problèmes de santé mentale périnatale. En ce qui concerne la DPN, les facteurs nutritionnels et génétiques représentent des champs potentiellement fructueux en vue de recherches plus poussées. Quant à ce qui a été traité dans le champ de la prématurité, le lien entre l'anxiété liée à la grossesse et la

durée de gestation ainsi que la pertinence des expériences de grossesses antérieures dans cette relation sont également des terrains importants à aborder dans le cadre de futures études.

Champs émergents de recherche

Pour conclure cette investigation touchant à diverses sphères de la santé mentale périnatale, quelques nouveaux champs émergents seront mentionnés. Ce regard se fonde sur un cadre conceptuel qui est centré sur le rôle des mères et de leur partenaire dans la parentalité, la famille et la communauté, et qui tient compte de l'importance effective des deux parents dans les familles duo-parentales.

La dépression périnatale paternelle. Désormais, les pères s'impliquent davantage dans la grossesse de leur partenaire et sont présents à l'accouchement. Ils assument environ un tiers des responsabilités de la garde des enfants [230]. Les pères peuvent donc jouer un rôle de soutien pour la famille, mais cette implication peut également mener à des tensions [231]. Les estimations de la prévalence de la DPN paternelle varient beaucoup, avec des résultats qui se situent entre 10,4 % [232] et 25,5 % [231]. Ce qui est clair à la lecture de la littérature scientifique, c'est que le taux de DPN est plus élevé parmi les hommes dont la partenaire vit une DPN elle-même. En fait, la DPN maternelle est le prédicteur le plus puissant de la DPN paternelle [231, 233]. Jusqu'à maintenant, les études montrent qu'une dépression chez le père peut avoir des effets néfastes sur le développement de l'enfant [234-236], mais ces effets peuvent différer des effets de la dépression maternelle [237]. Il reste du travail à faire pour déterminer la meilleure façon de gérer les défis de la santé mentale paternelle.

La santé mentale périnatale chez les mères homosexuelles. Les personnes homosexuelles ont un risque au moins deux fois plus élevé de souffrir de troubles affectifs comparativement aux personnes dites hétérosexuelles [238, 239]. En effet, il semblerait que les probabilités de souffrir de certaines formes de discrimination [240] et d'avoir un soutien social réduit, particulièrement venant des familles élargies [239, 241] soient plus grandes chez les femmes en couple avec d'autres femmes. D'un autre

côté, les mères homosexuelles sont moins sujettes aux grossesses non planifiées, et paraissent avoir tendance à partager les responsabilités qui incombent à la parentalité de façon plus égale que les parents hétérosexuels [239, 242]. Pourtant, celles-ci demeurent une population sous-étudiée [240, 241]. Les difficultés de la recherche auprès de cette population comprennent le recrutement d'échantillons suffisamment grands, l'identification de groupes de comparaison appropriés et la validation des échelles de mesure [242].

Les grossesses multiples. Entre 1981 et 1997, le taux de naissances jumelées au Canada a augmenté de 28 %, tandis que le taux de triplés et de grossesses d'ordre supérieur s'est presque multiplié par 3 [243]. Cette tendance est encore plus marquée dans d'autres pays [243]. Des augmentations plus récentes ont également été observées [244, 245], notamment au Canada [246]. Entre 30 % et 50 % des grossesses jumelées et 75 % des grossesses triplées résultent d'un traitement avec des technologies de procréation assistée [247], mais un quart, voire jusqu'à un tiers, de l'augmentation dans le taux des grossesses multiples est attribué à une hausse de l'âge maternel, et ce, avant même de tenir compte de l'utilisation cette technologie [243].

Les grossesses multiples impliquent des risques drastiquement élevés de complications telles que la NP [243, 247]. Pourtant, les effets sur la santé mentale de la mère sont parfois ignorés dans le programme de recherche sur les grossesses multiples [248]. Les femmes dans cette situation présentent des risques élevés de troubles de santé mentale, comme le stress et la dépression périnatale [248-251]. Il reste à confirmer plus précisément quels sont les risques chez cette population de développer ces problèmes, à assurer un transfert de connaissances et un soutien émotionnel pour la femme et sa famille [252], ainsi qu'à tenir compte des coûts associés à la santé mentale encourus par la mère dans l'estimation des coûts totaux des grossesses multiples [253].

Études de la santé mentale périnatale avec la cohorte 3D

L'Étude 3D se présente comme une ressource utile pour des projets de recherche portant sur la santé mentale dépassant les recherches montrées dans cette thèse. Les données de la cohorte 3D comprennent des mesures psychosociales des mères s'étalant jusqu'à deux ans après l'accouchement, qui permettront des études longitudinales sur la santé mentale postnatale. Après la naissance du nourrisson, la santé mentale maternelle et le développement de l'enfant s'influencent mutuellement [254254, 255]. Ainsi, des devis longitudinaux rendent possible la décortication de ces effets, notamment grâce à des études *cross-lag*. Des mesures psychosociales sur les partenaires sont aussi disponibles, ce qui permettra une riche gamme d'études sur la santé mentale paternelle.

Le projet 3D comprend aussi une abondance de spécimens biologiques. Ces échantillons faciliteront la continuation de l'exploration des liens entre le stress psychosocial et le stress biologique. Par exemple, des mesures du microbiome vaginal pourraient mener à une compréhension plus sophistiquée des liens entre le stress psychosocial et l'infection prénatale, comme discuté dans le chapitre 3. La collecte des échantillons biologiques des enfants est particulièrement importante, puisqu'ils rendent possible l'examen des rapports existant entre les taux d'hormones de stress chez la mère et l'enfant. Par exemple, l'analyse des relations entre le cortisol maternel et celui de l'enfant est actuellement en planification. Finalement, la collecte d'ADN chez le trio entier (mère, père et enfant) permettra des études sur la génétique et l'épigénétique familiale. D'importance certaine pour la santé mentale, l'Étude 3D peut servir de ressource afin de mieux comprendre les rôles joués par les facteurs génétiques et sociaux quant aux liens entre les problèmes de la santé mentale des parents et ceux des enfants.

Conclusion

La santé mentale périnatale demeure à l'intersection de deux aspects critiques de la santé. Cette thèse a passé en revue plusieurs facettes de la santé mentale périnatale. Elle comprend deux revues de la littérature et a présenté et interprété des résultats émanant de deux études liées à la cohorte 3D et portant sur une partie des enjeux discutés. Elle a également suggéré des directions futures pour la recherche dans ce domaine. Dans une étude menée avec rigueur, nous n'avons pas trouvé des liens importants entre le SPG et la NP, malgré la grande taille d'échantillon et l'examen des variables possiblement modératrices. Cette étude met le stress en contexte avec d'autres facteurs de risque pour la NP, ce qui pourrait offrir des pistes pour mener des investigations futures plus fructueuses. En tenant compte de ce qui a été couvert dans le présent travail, il serait judicieux que les futures études sur le stress et les issues de naissance valident nos résultats au sein des populations à risque élevé, et examinent les mesures biologiques du stress. Élucider les mécanismes sous-jacents des autres facteurs de risque plus importants de la NP serait également salutaire. Notre examen des antécédents de l'anxiété liée à la grossesse a révélé des associations de taille modeste liant l'issue d'une grossesse précédente avec la santé mentale pendant une grossesse subséquente. Ainsi, ces résultats peuvent servir à orienter le cadre conceptuel de l'anxiété liée à la grossesse dans les recherches futures ainsi que dans la pratique clinique. D'abord, en ce qui concerne la recherche, il serait important de déterminer dans quelle mesure l'anxiété liée à la grossesse agit comme marqueur pour d'autres facteurs de risque, étant donné que cela n'a pas reçu beaucoup d'attention jusqu'à présent. En effet, bien que l'anxiété prénatale constitue un problème mal reconnu, son rôle de prédicteur direct de mauvaises issues de grossesse devrait probablement être nuancé dans la recherche périnatale. Finalement, du côté clinique, il y aurait lieu de porter une attention aux issues des grossesses antérieures dans les outils de dépistage afin d'aider à identifier les patientes présentant un haut risque de développer des problèmes de santé mentale périnatale.

Étant donné que les problèmes traités dans la thèse comprennent des composantes biologiques, psychologiques et interpersonnelles, une approche transdisciplinaire s'impose. Avec un cadre de recherche centré sur la famille et un partage des connaissances et des techniques entre l'obstétrique, l'épidémiologie, la psychologie, la psychiatrie ainsi que d'autres disciplines, la santé de la mère peut être optimisée, ce qui à son tour permettra un réel épanouissement du potentiel de l'enfant.

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Annexe 1 : Références complètes, chapitre 3

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Annexe 2 : Questionnaire 1A, Étude de cohorte 3D

IRNPQEO Étude 3D

QUESTIONNAIRE 1A - Questionnaire maternel initial (entre 8 0/7 et 13 6/7 semaines)

Jour	Mois	Année	Centre	ID	Monogramme
☐☐	☐☐☐	☐☐☐☐	☐☐	☐☐☐	☐☐☐

ANTECEDENTS MEDICAUX

ANTECEDENTS OBSTETRICAUX

1. Avez-vous déjà été enceinte avant cette grossesse?

☐0 Non ➢ Allez à la section ANTÉCÉDENTS NON-OBSTÉTRICAUX ☐1 Oui ➢ Précisez

Si ***oui***, combien de grossesses avez-vous eues, quelle que soit l'issue, en incluant la grossesse actuelle? ☐☐

2. Âge à la première grossesse ☐☐

Veuillez décrire chacune de vos grossesses passées et l'état de chaque bébé (de la plus ancienne à la plus récente) en complétant le ***questionnaire 1C – Antécédents Obstétricaux****.*

ANTÉCÉDENTS NON-OBSTÉTRICAUX

Avez-vous l'une des maladies suivantes ? (cochez toutes les réponses qui s'appliquent)

Maladie/ Symptôme	Dans le passé (avant la grossesse actuelle)	Présentement (durant la grossesse actuelle)
3. Asthme	☐0 Non ☐1 Oui ☐99 Ne sait pas	☐0 Non ☐1 Oui ☐99 Ne sait pas
4. Diabète (indiquez le type) ☐0 Type I ☐1 Type II	☐0 Non ☐1 Oui ☐99 Ne sait pas	☐0 Non ☐1 Oui ☐99 Ne sait pas
5. Dysfonctionnement thyroïdien ☐0 Hypothyroïdie ☐1 Hyperthyroïdie ☐2 Autre	☐0 Non ☐1 Oui ☐99 Ne sait pas	☐0 Non ☐1 Oui ☐99 Ne sait pas
6. Malformation cardiaque congénitale ➢Si **oui,** précisez : _____	☐0 Non ☐1 Oui ☐99 Ne sait pas	☐0 Non ☐1 Oui ☐99 Ne sait pas
7. Cholestérol élevé	☐0 Non ☐1 Oui ☐99 Ne sait pas	☐0 Non ☐1 Oui ☐99 Ne sait pas
8. Haute pression sanguine	☐0 Non ☐1 Oui ☐99 Ne sait pas	☐0 Non ☐1 Oui ☐99 Ne sait pas
9. Pneumonie	☐0 Non ☐1 Oui ☐99 Ne sait pas	☐0 Non ☐1 Oui ☐99 Ne sait pas

	Dans le passé (avant la grossesse actuelle)	Présentement (durant la grossesse actuelle)
10. Autre maladie cardiovasculaire: ➢Si **oui,** précisez **:**_____	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas
11. Thrombose véneuse profonde	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas
12. Hépatite (jaunisse)	☐ A ☐ B ☐ C ☐ Autre ☐ Non ☐ Ne sait pas	☐ A ☐ B ☐ C ☐ Autre ☐ Non ☐ Ne sait pas
13. Autre problème gastro-intestinal ➢Si **oui,** précisez **:**_____	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas
14. Anémie	☐$_2$ Carence en fer ☐$_1$ Autre carence en vitamines ☐$_0$ Aucune ☐$_{99}$ Ne sait pas	☐$_2$ Carence en fer ☐$_1$ Autre carence en vitamines ☐$_0$ Aucune ☐$_{99}$ Ne sait pas
15. Infection du tractus génital / Maladie transmise sexuellement (cochez toutes les réponses qui s'appliquent)	☐ Gonnorhée ☐ Chlamydia ☐ Condylome ☐ Autre ☐ Herpès ☐ Aucune	☐ Gonnorhée ☐ Chlamydia ☐ Condylome ☐ Autre ☐ Herpès ☐ Aucune
16. Pathologie du col de l'utérus (Conisation du col utérin ou résection à l'anse diathermique)	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas
17. Infection rénale	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas
18. Dépression majeure / Psychose ➢Si **oui,** précisez: _____	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas
19. Rhume et symptômes d'allure grippale	Ne s'applique pas	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas
20. Chirurgie bariatrique	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas
21. Convulsions	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas
22. Fièvre	Ne s'applique pas	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas
23. Autre (non-décrit ci-haut): _____	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas

Si vous avez pris des médicaments (comprimés/mélanges, suppositoires, pompes, crèmes, etc.) à cause des maladies ou problèmes de santé ci-dessus, veuillez compléter le **journal des médicaments et des suppléments nutritionnels s (MML)** et y indiquer le nom du ou des médicament(s) et à quel moment vous le/les avez consommé(s).

VACCINATION

1. Avez-vous déjà été vaccinée pour le virus du papillome humain (VPH) ? ☐$_0$ Non ☐$_1$ Oui ➢Précisez:

Indiquez la date approximative de votre vaccination (*mmm /aaaa)* ☐☐☐ / ☐☐☐☐

Veuillez indiquer le nom du vaccin que vous avez reçu.

☐$_0$ Gardasil (Quadrivalent, 4 types) ☐$_1$ Cervarix (Bivalent, 2 types) ☐$_{99}$ Ne sait pas

2. Avez-vous été vaccinée contre la grippe A H1N1 ? ☐$_0$ Non ☐$_1$ Oui ➢Précisez :

Indiquez la date approximative de votre vaccination *(jj/mmm/aaaa)* ☐☐/ ☐☐☐ / ☐☐☐☐

Quel type de vaccin avez-vous reçu ? ☐$_1$ Avec adjuvent ☐$_0$ Sans adjuvent ☐$_{99}$ Ne sait pas

Indiquez le nom du vaccin que vous avez reçu

☐$_0$ Arepanrix™ H1N1 ☐$_1$ Panvax™ ☐$_{99}$ Ne sait pas

3. Avez-vous été vaccinée contre la grippe saisonnière ? ☐$_0$ Non ☐$_1$ Oui ➢Précisez:

Indiquez la date approximative de votre dernier vaccin *(mmm/ aaaa)* ☐☐☐ / ☐☐☐☐

ANTÉCÉDENTS FAMILIAUX

Est-ce que votre **mère** ou **sœur(s)** (si vous en avez une) ont ou ont eu une des maladies suivantes ?

Maladie / Syndrome	**MÈRE** **(de la femme enceinte)** ☐$_{97}$ N/A	**SOEUR(S)** **(de la femme enceinte)** ☐$_{97}$ N/A
1. Asthme	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas	☐$_0$ Non ☐$_0$ Oui ☐$_{99}$ Ne sait pas
2. Diabète (Préciser le type)	☐$_1$ Type I ☐$_2$ Type II ☐$_0$ Non ☐$_{99}$ Ne sait pas	☐$_1$ Type I ☐$_2$ Type II ☐$_0$ Non ☐$_{99}$ Ne sait pas
3. Diabète gestationnel	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas
4. Hypertension chronique	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas
5. Hypertension gravidique	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas
6. Pré-éclampsie ou éclampsie	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas
7. Cholestérol élevé	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas
8. Accouchement d'un enfant mort-né	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas

Maladie / Syndrome	MÈRE (de la femme enceinte) ☐97 N/A	SOEUR(S) (de la femme enceinte) ☐97 N/A
9. Mort d'un enfant de moins d'un an	☐0 Non ☐1 Oui ☐99 Ne sait pas	☐0 Non ☐1 Oui ☐99 Ne sait pas
10. Accouchement d'un enfant de moins de 2,5 kg (5,5 lbs)	☐0 Non ☐1 Oui ☐99 Ne sait pas	☐0 Non ☐1 Oui ☐99 Ne sait pas
11. Accouchement d'un enfant prématuré (<37 sem)	☐0 Non ☐1 Oui ☐99 Ne sait pas	☐0 Non ☐1 Oui ☐99 Ne sait pas
12. A eu ≥ 2 avortements spontanés ou ≥ 2 avortements tardifs	☐0 Non ☐1 Oui ☐99 Ne sait pas	☐0 Non ☐1 Oui ☐99 Ne sait pas
13. A eu un enfant avec une malformation congénitale (Inclure les interruptions de grossesse, les enfants mort-nés et les naissances vivantes) **Précisez**	☐0 Non ☐1 Oui ☐99 Ne sait pas _____	☐0 Non ☐1Oui ☐99 Ne sait pas _____

Est-ce que votre **père** ou **frère** (si vous en avez un) ont ou ont eu une des maladies suivantes ?

Maladie/ Syndrome	PÈRE (de la femme enceinte) ☐97 N/A	FRÈRE (de la femme enceinte) ☐97 N/A
14. Asthme	☐0 Non ☐1 Oui ☐99 Ne sait pas	☐0 Non ☐1 Oui ☐99 Ne sait pas
15. Diabète (préciser le type)	☐1 Type I ☐2 Type II ☐0 Non ☐99 Ne sait pas	☐1 Type I ☐2 Type II ☐0 Non ☐99 Ne sait pas
16. Hypertension artérielle	☐0 Non ☐1 Oui ☐99 Ne sait pas	☐0 Non ☐1 Oui ☐99 Ne sait pas
17. Mort d'un enfant de moins d'un an	☐0 Non ☐1 Oui ☐99 Ne sait pas	☐0 Non ☐1 Oui ☐99 Ne sait pas
18. Cholestérol élevé	☐0 Non ☐1 Oui ☐99 Ne sait pas	☐0 Non ☐1 Oui ☐99 Ne sait pas
19. A eu un enfant avec une malformation congénitale (Inclure les interruptions de grossesse, les enfants mort-nés et les naissances vivantes) **Précisez**	☐0 Non ☐1 Oui ☐99 Ne sait pas _____	☐0 Non ☐1 Oui ☐99 Ne sait pas _____

20. Êtes-vous parente avec votre conjoint?

☐0 Non ☐1 Oui ➢ Précisez le lien : _____

GROSSESSE ACTUELLE

ÂGE GESTATIONNEL

1. Date de vos dernières menstruations *(jj/mmm/aaaa)* ☐☐/ ☐☐☐ / ☐☐☐☐ ☐99 Ne sait pas

   (La première journée de vos menstruations.)

Important: ➢ Complétez maintenant le questionnaire US-1

ÉVOLUTION DE LA GROSSESSE ACTUELLE

3. Depuis le début de votre grossesse actuelle, avez-vous eu des complications ? ☐0 Non ☐1 Oui ➢ Précisez :

   Quelle(s) complication(s) avez-vous eu durant cette grossesse ?

   ☐0 Vomissements répétés et perte de poids

   ☐1 Saignements vaginaux

   ☐2 Vaginose bactérienne traitée ➢ Précisez la date *(jj/ mmm/ aaaa)* ☐☐/ ☐☐☐/ ☐☐☐☐

   ☐3 Autre

CONTRACEPTION/ INFERTILITÉ

4. Est-ce que votre partenaire et vous avez essayé d'avoir un enfant pendant une période de **6 mois ou plus** sans succès ?

   ☐0 Non ☐1 Oui ➢ Précisez

   Avez-vous déjà essayé, votre partenaire et vous, d'avoir un enfant pendant une période **d'au moins 1 an** sans succès ?

   ☐0 Non ☐1 Oui

5. Combien de temps cela vous a-t-il pris pour devenir enceinte de votre grossesse actuelle ? ☐☐ mois

6. Si vous avez déjà été enceinte, combien de temps aviez-vous mis pour devenir enceinte ? ☐☐ mois ☐97 N/A

7. Est-ce qu'un médecin ou autre professionnel de la santé a diagnostiqué chez vous et/ou chez votre partenaire un problème de fertilité ?

   ☐0 Non ☐1 Oui ➢ Indiquez la cause de ce problème de fertilité. (Cochez toutes les réponses qui s'appliquent)

   Causes féminines

   ☐ Facteurs tubaires (trompes bloquées ou dysfonctionnelles)

☐ Dysovulation / anovulation
☐ PCOS (syndrome des ovaires polykystiques)
☐ Endométriose
☐ Réserve ovarienne réduite / insuffisance ovarienne prématurée (spontanée ou causée par un traitement)

☐ Anomalie du mucus cervical (mucus cervical hostile, insuffisance du mucus cervical)
☐ Malformation de l'utérus
☐ Autre cause féminine, veuillez préciser : _____
☐ Raison inconnue

Causes masculines

☐ Absence de sperme
☐ Incapacité à déposer le sperme (dysfonction érectile/ éjaculatoire)
☐ Anomalie des spermatozoïdes (peu de spermatozoïdes ou spermatozoïdes de mauvaise qualité)

☐ Autre cause masculine, précisez: _____
☐ Raison inconnue

8. Avez-vous eu recours à des méthodes de procréation assistée ou avez-vous utilisé des médicaments déclenchant l'ovulation afin d'être enceinte de **votre grossesse actuelle** ?

☐$_0$ Non ➢ Allez à question 9

☐$_1$Oui ➢ Précisez (cochez toutes les réponses qui s'appliquent) ET

☐$_{98}$ Refuse de répondre ➢ Demandez à la patiente de compléter le formulaire de consentement d'accès au dossier médical de fertilité

Stimulation ovarienne

☐ Stimulation ovarienne par voie orale (ex. Clomid ®, Serophene ®)

☐ Stimulation ovarienne par voie injectable (ex. Repronex ®, Follistim ®, Gonal-F ®, Menopur ®)

☐ Médicament injectable pour déclencher l'ovulation (ex. Ovidrel ®, Profasi ®, Pregnyl ®, Novarel ®)

☐ Autre médicament facilitant la conception (ex. Metformin ®, Provera ®, Lupron ®)

Insémination intra-utérine (IIU)

☐ Avec sperme du partenaire
☐ Avec sperme du donneur

Fécondation *in-vitro* (FIV)

☐ Avec ICSI (Injection intra-cytoplasmique du spermatozoïde)
☐ Sans ICSI

Maturation *In Vitro* (MIV)

☐ Sans ICSI
☐ Avec ICSI

Autres

☐ Transfert d'embryons congelés (TEC)
☐ Transfert intratubaire de zygotes (ZIFT)
☐ Transfert intratubaire des gamètes (GIFT)
☐ Don de sperme
☐ Don d'ovules
☐ Don d'embryons
☐ Éclosion embryonnaire assistée (Hatching)

9. Le père biologique du bébé a-t-il reçu des traitements d'infertilité **avant cette grossesse dans le but de vous aider à devenir enceinte ?**

☐$_0$ Non ☐$_1$ Oui ➢Précisez (Cochez toutes les réponses qui s'appliquent)

☐ Correction de varicocèle
☐ Acupuncture
☐ Chirurgie
☐ Médicament pour l'aider à maintenir une érection
☐ Ne sait pas
☐ Inversion de vasectomie
☐ Analyse de sperme
☐ Conseil médical
☐ Médicament pour augmenter la qualité de son sperme
☐ Refuse de répondre

10. Avez-vous cessé votre dernière méthode de contraception **avant le début de votre grossesse,** ou cette grossesse est-elle le résultat d'un échec de contraception ?

☐$_0$ Arrêt de contraception avant la grossesse ☐$_1$ Échec de contraception ☐$_{97}$ N/A
☐$_2$ Incertain ☐$_{98}$ Refuse de répondre

11. Si vous **n'utilisiez pas de méthode de contraception avant cette grossesse**, souhaitiez-vous devenir enceinte ?

☐$_0$ Non ➢Précisez ☐$_1$ Oui ☐$_{99}$ Ne sait pas ☐$_{98}$ Refuse de répondre

Si ***non***, malgré le fait que vous ne souhaitiez pas devenir enceinte, aviez-vous l'intention de continuer la grossesse si vous deveniez enceinte?

☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas ☐$_{98}$ Refuse de répondre

12. À quel point étiez-vous motivée à devenir enceinte à ce moment-là?

☐$_0$ Pas du tout ☐$_1$ Un peu ☐$_2$ Raisonnablement ☐$_3$ Significativement ☐$_4$ Complètement

13. Avez-vous consommé des médicaments afin de maintenir l'évolution de **cette grossesse** ?

☐$_0$ Non ☐$_1$ Oui ➢Précisez (Cochez toutes les réponses qui s'appliquent)

☐ Progestérone orale
☐ Progestérone en suppositoire vaginal

☐ Progestérone par injection

☐ Anticoagulants (ex. Heparin ®, Loveno ®)

☐ Faible dose d'Aspirine (Aspirine pour enfant)

14. En dehors de vos frères et sœurs, est-ce qu'un membre de votre famille (parents, grand-parents, tantes, oncles, nièces, neveux et cousins, si applicable) a déjà tenté de concevoir pendant une période **d'au moins 6 mois** sans succès ?

☐$_0$ Non ☐$_1$ Oui ➢ Précisez qui était concerné: _____ ☐$_{99}$ Ne sait pas

15. Est-ce qu'un membre de votre famille a tenté de concevoir pendant une période **d'un an ou plus** sans succès ?

☐$_0$ Non ☐$_1$ Oui ➢ Précisez qui était concerné : _____ ☐$_{99}$ Ne sait pas

MÉDECIN TRAITANT POUR CETTE GROSSESSE

1. Quel professionnel de la santé assure le suivi de votre grossesse ?

☐$_0$ MD / Obstétricien ☐$_1$ MD / Médecin de famille ☐$_2$ Infirmière sage-femme

☐$_3$ Autre sage-femme ☐$_4$ Autre, précisez : _____

MÉDICATION

1. Avez-vous consommé des médicaments dans **les 3 mois précédant ou depuis le début de votre grossesse** ?

☐$_0$ Non ☐$_1$Oui ➢ Veuillez compléter le JOURNAL DES MÉDICAMENTS ET DES SUPPLÉMENTS NUTRITIONNELS – MÈRE (MML)

SUPPLÉMENTS NUTRITIONNELS

1. Avez-vous déjà consommé des vitamines, minéraux ou suppléments diététiques dans **les 3 mois précédant ou depuis le début de votre grossesse** ?

☐$_0$ Non ➢ Allez à la SECTION TABAGISME ☐$_1$Oui ➢ Veuillez compléter le JOURNAL DES MÉDICAMENTS ET DES SUPPLÉMENTS NUTRITIONNELS – MÈRE (MML)

SECTION TABAGISME

1. EXPOSITION À LA FUMÉE PRIMAIRE

Je vais maintenant vous poser des questions sur la consommation de cigarettes. Par cigarettes, nous entendons les cigarettes prêtes à l'usage et celles que vous roulez vous-même, SAUF les cigares, les cigarillos, la marijuana et la pipe.

1.1. Avez-vous fumé au moins 100 cigarettes ou plus **au cours de votre vie** (environ 4 paquets) ?

☐$_0$ Non ➢ Allez à la section **2.** EXPOSITION À LA FUMÉE SECONDAIRE ☐$_1$ Oui ☐$_{99}$ Ne sait pas ☐$_{98}$ Refuse de répondre

1.2. À quel âge avez-vous fumé votre première cigarette entière ? ☐☐ ans

1.3. **<u>Dans l'année qui a précédé votre grossesse</u>**

1.3.1. Combien de jours avez-vous fumé une cigarette ou plus ?

☐ Nombre de jours par semaine **<u>ou</u>** ☐☐ Nombre de jours par mois **<u>ou</u>** ☐☐☐ Nombre total de jours dans l'année **<u>ou</u>**

☐☐☐ Nombre de mois durant l'année ☐$_{99}$ Ne sait pas ☐$_{98}$ Refuse de répondre

1.3.2. Les jours où vous fumiez, combien de cigarettes fumiez-vous habituellement ?

☐☐ Nombre de cigarettes ☐$_{99}$ Ne sait pas ☐$_{98}$ Refuse de répondre

1.3.3. Avez-vous cessé de fumer **avant de devenir enceinte (dernières menstruations)**?

☐$_0$ Non ☐$_1$ Oui ➢ Allez à 1.5

1.4. **<u>Depuis le début de votre grossesse</u>**, (*c.-à.-d.* depuis la première journée de vos dernières menstruations)

1.4.1. Combien de jours avez-vous fumé une cigarette ou plus?

☐ Nombre de jours par semaine **<u>ou</u>** ☐☐ Nombre de jours par mois **<u>ou</u>** ☐☐☐ Nombre total de jours depuis le début de la grossesse

☐$_{99}$ Ne sait pas ☐$_{98}$ Refuse de répondre

1.4.2. Les jours où vous fumez (fumiez), combien de cigarettes fumez-vous (fumiez-vous) habituellement ?

☐☐ Cigarettes / jour ☐$_{99}$ Ne sait pas ☐$_{98}$ Refuse de répondre

1.5. Date d'arrêt ? (*jj/ mmm/ aaaa)* ☐☐ /☐☐☐ /☐☐☐☐

2. EXPOSITION À LA FUMÉE SECONDAIRE

Je vais maintenant vous poser des questions sur votre exposition à la fumée secondaire <u>depuis le début de votre grossesse</u>, c.-à.-d.. depuis le premier jour de vos dernières menstruations.

2.1. En comptant les membres de votre ménage et les visiteurs réguliers, combien de personnes fument à l'intérieur de votre domicile, chaque jour ou presque chaque jour ?

☐☐ Nombre de personnes

2.2. En général, à l'exception de votre propre fumée... (*INTERVIEWER: Lisez les catégories à la participante)*

	2.2.1. Avez-vous été exposée à la fumée des autres à l'intérieur de votre domicile **depuis le début de votre grossesse** ?	2.2.2. En excluant la fumée secondaire à laquelle vous êtes exposée à la maison, à quelle fréquence avez-vous été exposée à de la fumée secondaire ?
Chaque jour	☐4	☐4
Presque chaque jour	☐3	☐3
Au moins une fois par semaine	☐2	☐2
Au moins une fois par mois	☐1	☐1
Jamais	☐0	☐0
Ne sait pas	☐99	☐99
Refuse de répondre	☐98	☐98

2.3. En général, à l'exception de votre propre fumée, combien de cigarettes sont fumées à chaque jour dans votre domicile **depuis le début de votre grossesse** ? Ex. Si le père fume 5 cigarettes et qu'une autre personne en fume 3, le total est de 8 cigarettes (*INTERVIEWER: Lisez les catégories à la participante).*

☐0 Aucune ☐1 1 à 10 cigarettes ☐2 11 à 20 cigarettes ☐3 21 à 30 cigarettes ☐4 31 à 40 cigarettes

☐99 Ne sait pas ☐98 Refuse de répondre

2.4. **Depuis le début de votre grossesse,** avez-vous été exposée à la fumée des autres, chaque jour ou presque chaque jour...

	2.4.1. Dans une voiture ou dans un autre véhicule privé ?	2.4.2. Dans votre lieu de travail ?
Non	☐0	☐0
Oui	☐1	☐1
Ne sait pas	☐99	☐99
Refuse de répondre	☐98	☐98

3. EXPOSITION À LA FUMÉE TERTIAIRE

Je vais maintenant vous poser des questions sur votre exposition à la fumée tertiaire depuis le début de votre grossesse, *c.-à.-d.* depuis le premier jour de vos dernières menstruations. (La fumée tertiaire correspond à un environnement contaminé avec de la fumée de **TABAC**, sans que personne n'y **FUME** durant votre présence)

3.1. Avez-vous été exposée à de la fumée tertiaire chaque jour ou presque chaque jour dans votre domicile ?

☐$_0$ Jamais ☐$_1$ Au moins une fois par mois ☐$_2$ Au moins une fois par semaine ☐$_3$ Presque chaque jour ☐$_4$ Chaque jour

☐$_{99}$ Ne sait pas ☐$_{98}$ Refuse de répondre

SECTION CONSOMMATION D'ALCOOL

J'aimerais maintenant vous poser quelques questions sur votre consommation d'alcool. *Lorsqu'on parle d'un « verre » on entend : une bouteille ou une canette de bière, ou un verre de bière en fût ; un verre de vin ou de boisson rafraîchissante au vin (« cooler ») ; un verre ou un cocktail contenant une once et demie de spiritueux.*

1. **Dans l'année qui a précédé votre grossesse,** à quelle fréquence avez-vous ...

	1.1. Consommé des boissons alcoolisées ?	1.2. Consommé 5 boissons alcoolisées ou plus en une même occasion ?
Chaque jour	☐$_7$	☐$_7$
4 à 6 fois par semaine	☐$_6$	☐$_6$
2 à 3 fois par semaine	☐$_5$	☐$_5$
1 fois par semaine	☐$_4$	☐$_4$
2 à 3 fois par mois	☐$_3$	☐$_3$
1 fois par mois	☐$_2$	☐$_2$
Moins de 1 fois par mois	☐$_1$	☐$_1$
Jamais	☐$_0$	☐$_0$
Ne sait pas	☐$_{99}$	☐$_{99}$
Refuse de répondre	☐$_{98}$	☐$_{98}$

2. En pensant à la **dernière semaine**, c'est-à-dire entre [la date d'il y a une semaine] et hier, est-ce que vous avez bu de la bière, du vin, un spiritueux ou toute autre boisson alcoolisée ?

☐$_0$ Non ➢ Allez à Q5 ☐$_1$ Oui ☐$_{99}$ Ne sait pas ☐$_{98}$ Refuse de répondre

3. **En remontant à partir d'hier,** c'est-à-dire [nom de jour], combien de verres avez-vous bus ?

   ➢ *INTERVIEWER :* Posez Q3 sept fois, une fois pour chaque jour de la semaine, en allant à rebours à partir d'hier

Dimanche	Lundi	Mardi	Mercredi	Jeudi	Vendredi	Samedi
☐☐	☐☐	☐☐	☐☐	☐☐	☐☐	☐☐

☐$_{99}$ Ne sait pas ☐$_{98}$ Refuse de répondre

4. Y a-t-il eu une occasion spéciale durant cette dernière semaine ?

   ☐$_{0}$ Non ☐$_{1}$ Oui

5. **Depuis le début de votre grossesse**, c'est-à-dire depuis la première journée de vos dernières menstruations, votre consommation d'alcool a-t-elle été supérieure, à peu près la même ou inférieure à la quantité que vous consommiez habituellement ?

   ☐$_{2}$ Supérieure ☐$_{1}$ Environ la même ☐$_{0}$ Inférieure

   ☐$_{99}$ Ne sait pas ☐$_{98}$ Refuse de répondre

6. **Depuis le début de votre grossesse,** à quelle fréquence avez-vous ...

➢ Si la participante répond *0* à 6.1, passez 6.2 et allez à la question 8.

	6.1. Consommé des boissons alcoolisées ?	6.2. Consommé 5 boissons alcoolisées ou plus en une seule occasion ?
Nombre de jours par semaine **ou**	☐	☐
Nombre de jours par mois **ou**	☐☐	☐☐
Nombre total de jours depuis le début de la grossesse	☐☐☐	☐☐☐
Ne sait pas	☐99	☐99
Refuse de répondre	☐98	☐98

7. Les journées où vous avez consommé de l'alcool, **depuis le début de votre grossesse**, combien de verres buviez-vous habituellement ?

➢ *Lorsqu'on parle d'un « verre » on entend : une bouteille ou une canette de bière, ou un verre de bière en fût ; un verre de vin ou de boisson rafraîchissante au vin (« cooler ») ; un verre ou un cocktail contenant une once et demie de spiritueux.*

☐☐ Verre(s) ☐99 Ne sait pas ☐98 Refuse de répondre

8. Je comprends que vous ne consommez généralement pas d'alcool car vous êtes enceinte, mais vous est-il arrivé de consommer de l'alcool au cours d'occasions spéciales, telles que des anniversaires ou rassemblements familiaux ?

☐0 Non ➢Allez à Q9 ☐1 Oui ➢ Continuez ☐99 Ne sait pas ☐98 Refuse de répondre

8.1. Combien de consommations d'alcool avez-vous prises lors de ces occasions ?

☐☐ Verre(s) ☐99 Ne sait pas ☐98 Refuse de répondre

8.2. Combien de fois est-ce arrivé ?

☐☐☐ Occasion(s) ☐99 Ne sait pas ☐98 Refuse de répondre

9. Combien devez-vous consommer de verres pour sentir l'effet de l'alcool ?

☐☐ Verre(s) ☐99 Ne sait pas ☐98 Refuse de répondre

	Non	Oui	Ne sait pas	Refuse de répondre
10. Les gens vous ont-ils déjà agacée en critiquant votre consommation d'alcool ?	☐0	☐1	☐99	☐98
11. Avez-vous déjà eu l'impression que vous devriez réduire votre consommation d'alcool ?	☐0	☐1	☐99	☐98
12. Vous est-il déjà arrivé de prendre un verre en vous levant pour calmer vos nerfs ou vous débarrasser d'une gueule de bois ?	☐0	☐1	☐99	☐98

SECTION CAFÉ, THÉ ET BOISSONS ÉNERGISANTES

Durant l'année précédent votre grossesse, avez consommé régulièrement (c.-à.-d. au moins une fois par semaine)...

			Si oui		
	Non	Oui	Combien de tasses/ jour ?	Combien de jours/ semaine ?	Avez-vous cessé de consommer cette boisson 3 mois ou plus avant de devenir enceinte ?
1. Café régulier ?	☐0	☐1	☐☐	☐	☐0 Non ☐1 Oui
2. Café décaféiné ?	☐0	☐1	☐☐	☐	☐0 Non ☐1 Oui
3. Thé régulier / noir ?	☐0	☐1	☐☐	☐	☐0 Non ☐1 Oui
4. Thé vert ?	☐0	☐1	☐☐	☐	☐0 Non ☐1 Oui
5. Tisane ?	☐0	☐1	☐☐	☐	☐0 Non ☐1 Oui
6. Autres thés ?	☐0	☐1	☐☐	☐	☐0 Non ☐1 Oui
7. Boissons gazeuses caféinées (ex. : Coke, Pepsi) ou du thé glacé ?	☐0	☐1	☐☐	☐	☐0 Non ☐1 Oui
8. Boissons énergisantes (ex. : Red Bull) ?	☐0	☐1	☐☐	☐	☐0 Non ☐1 Oui

Depuis le début de la grossesse, avez consommé régulièrement (c.-à.-d. au moins une fois par semaine)...

			Si Oui	
	Non	**Oui**	Combien de tasses/ jour?	Combien de jours/ semaine?
9. Café régulier ?	☐0	☐1	☐☐	☐
10. Café décaféiné ?	☐0	☐1	☐☐	☐
11. Thé régulier / noir ?	☐0	☐1	☐☐	☐
12. Thé vert ?	☐0	☐1	☐☐	☐
13. Tisane ?	☐0	☐1	☐☐	☐
14. Autres thés ?	☐0	☐1	☐☐	☐
15. Boissons gazeuses caféinées (ex. : Coke, Pepsi) ou du thé glacé ?	☐0	☐1	☐☐	☐
16. Boissons énergisantes (ex. : Red Bull)?	☐0	☐1	☐☐	☐

SECTION USAGE DE DROGUES ILLICITES

Je vais vous poser quelques questions au sujet de la consommation de drogues. Encore une fois, j'aimerais vous rappeler que tout ce que vous dites demeurera **strictement confidentiel**.

1. Avez-vous déjà pris ou essayé des drogues (p. ex. marijuana, cannabis, haschisch, cocaïne, speed, hallucinogènes, LSD, PCP, etc.) ?

   ☐0 Non ☐1 Oui ☐99 Ne sait pas ☐98 Refuse de répondre

   ➢ Si *Non*, *Ne sait pas* ou *Refuse de répondre***,** passez à la prochaine section

2. Avez-vous déjà pris ou essayé l'une des drogues suivantes ?

			Si Oui			
	Non	**Oui**	**Combien de fois depuis que vous êtes devenue enceinte ?**			
2.1 La marijuana, du cannabis ou du haschisch	☐0	☐1	☐ jours/ semaine	☐☐ jours/ mois	☐☐☐ Total jours depuis le début de la grossesse	☐98 Refus

2.2 De la cocaïne ou du crack	☐0	☐1	☐ jours/ semaine	☐☐ jours/ mois	☐☐☐ Total jours depuis le début de la grossesse	☐98 Refus
2.3 Du speed (amphétamines)	☐0	☐1	☐ jours/ semaine	☐☐ jours/ mois	☐☐☐ Total jours depuis le début de la grossesse	☐98 Refus
2.4 Des hallucinogènes tels que le LSD, le PCP, l'ecstasy (MDMA), la mescaline, le buvard ou autres drogues semblables	☐0	☐1	☐ jours/ semaine	☐☐ jours/ mois	☐☐☐ Total jours depuis le début de la grossesse	☐98 Refus
2.5 Inhalé de la colle, de l'essence ou d'autres solvants	☐0	☐1	☐ jours/ semaine	☐☐ jours/ mois	☐☐☐ Total jours depuis le début de la grossesse	☐98 Refus
2.6 De l'héroïne (ex. smack)	☐0	☐1	☐ jours/ semaine	☐☐ jours/ mois	☐☐☐ Total jours depuis le début de la grossesse	☐98 Refus

SECTION EMPLOI

1. Quelle est votre profession ? _____

2. Quelle était votre situation d'emploi lorsque vous êtes devenue enceinte ? Veuillez cocher toutes les réponses qui s'appliquent.

   ☐0 Employée à temps plein

   ☐1 Employée à temps partiel

   ☐2 Étudiante

   ☐3 Sans emploi

   ☐4 Femme au foyer

   ☐5 Autre, précisez : _____

   ➢Si vous **étiez sans emploi,** passez à la SECTION EXPOSITION ENVIRONNEMENTALE.

   2.1 Si vous étiez employée, veuillez indiquer le nombre d'heures travaillées par semaine: ☐☐ heures

3. Quel est votre horaire de travail ou d'étude ?

☐$_0$ Travail permanent de jour

☐$_1$ Travail permanent l'après-midi ou le soir

☐$_2$ Travail permanent de nuit

☐$_3$ Travail en quarts ou en rotation de quarts

☐$_4$ Aucun horaire fixe (travail supplémentaire, quarts supplémentaires, travail temporaire, etc.)

☐$_5$ Autre

4. **Depuis le début de votre grossesse**, avez-vous **cessé** de travailler ou d'étudier ?

☐$_0$ Non ➢ Allez à Q5 ☐$_1$ Oui ➢Précisez :

Quand avez-vous cessé ? *(jj/ mmm/ aaaa)* ☐☐/ ☐☐☐/ ☐☐☐☐

Pourquoi avez-vous cessé?

☐$_0$ Retrait préventif/ Départ

☐$_1$ Fin de contrat

☐$_2$ Congédiement

☐$_3$ Démission

☐$_4$ Problèmes de santé

☐$_5$ Autre, précisez: _____

5. **Depuis le début de votre grossesse**, avez-vous **réduit** votre nombre d'heures de travail ou d'étude ?

☐$_0$ Non ➢ Allez à Q6 ☐$_1$ Oui ➢Précisez :

Quand avez-vous réduit votre nombre d'heures de travail ou d'étude ? *(jj/ mmm/ aaaa)* ☐☐/ ☐☐☐/ ☐☐☐☐

Pendant combien d'heures par semaine travaillez-vous maintenant ? ☐☐ heures

Pourquoi avez-vous réduit vos heures ?

☐$_0$ Retrait préventif/ Départ

☐$_1$ Fin de contrat

☐$_2$ Congédiement

☐$_3$ Démission

☐$_4$ Problèmes de santé

☐$_5$ Autre, précisez : _____

6. Considérez-vous que votre emploi est stressant ?

☐$_0$ Non ☐$_1$ Oui

7. Durant votre grossesse, y a t il eu des évènements particuliers au travail tel que déversement de produit chimique, une fuite de gaz ?

☐$_0$ Non➢Allez à la section EXPOSITION ENVIRONNEMENTALE ☐$_1$ Oui ➢Précisez ☐$_{99}$ Ne sait pas

Précisez l'événement : _____

Aviez-vous été directement exposée ?

☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas

SECTION EXPOSITIONS ENVIRONNEMENTALES

	3 mois avant cette grossesse	Depuis le début de cette grossesse
1. Avez-vous déjà utilisé des produits capillaires (ex. teinture, permanente, défrisant, gel, etc.) ? ☐$_0$ Non (allez à Q2) ☐$_1$ Oui ☐$_{99}$ Ne sait pas (allez à Q2)		
Colorants capillaires	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas
Permanentes	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas
Produits défrisants	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas
Fixatifs ou gels	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas
2. Avez-vous déjà utilisé des produits pour les ongles ? ☐ Non (allez à Q3) ☐ Oui ☐ Ne sait pas (allez à Q3)		
Si ***oui,***	☐$_5$ Quotidiennement ☐$_2$ 1 fois/ mois ☐$_4$ 2-3 fois/semaine ☐$_1$ Moins d'une fois/ mois ☐$_3$1 fois/ semaine ☐$_0$ Jamais ou rarement	☐$_5$ Quotidiennement ☐$_2$ 1 fois/ mois ☐$_4$ 2-3 fois/semaine ☐$_1$ Moins d'une fois/ mois ☐$_3$1 fois/ semaine ☐$_0$ Jamais ou rarement
3. Avez-vous déjà utilisé du maquillage ex. crayon contour des lèvres, rouge à lèvres, fond de teint, mascara, fard à joues, ligneur, fard à paupières) ? ☐$_0$ Non (allez à Q4) ☐$_1$ Oui ☐$_{99}$ Ne sait pas (allez à Q4)		
Si ***oui,*** veuillez préciser: _____ _____	☐$_5$ Quotidiennement ☐$_2$ 1 fois/ mois ☐$_4$ 2-3 fois/semaine ☐$_1$ Moins d'une fois/ mois ☐$_3$1 fois/ semaine ☐$_0$ Jamais ou rarement	☐$_5$ Quotidiennement ☐$_2$ 1 fois/ mois ☐$_4$ 2-3 fois/semaine ☐$_1$ Moins d'une fois/ mois ☐$_3$1 fois/ semaine ☐$_0$ Jamais ou rarement
4. Utilisez-vous des produits de soin pour la peau (ex. : crème ou lotion hydratante)? ☐ Non (allez à Q5) ☐ Oui ☐ Ne sait pas (allez à Q5)		
Si ***oui***	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas	☐$_0$ Non ☐$_1$ Oui ☐$_{99}$ Ne sait pas
5. Utilisez-vous de la crème solaire ? ☐$_0$ Non (allez à Q6) ☐$_1$ Oui ☐$_{99}$ Ne sait pas (allez à Q6)		
Si *oui* , veuillez indiquer le facteur de protection solaire ☐$_0$ 15 ☐$_1$ 30 ☐$_2$ 45 ☐$_3$ 50 ☐$_4$ 60 ☐$_5$ 70 ☐$_6$ 80 ☐$_7$ 90	☐$_5$ Quotidiennement ☐$_2$ 1 fois/ mois ☐$_4$ 2-3 fois/semaine ☐$_1$ Moins d'une fois/ mois ☐$_3$1 fois/ semaine ☐$_0$ Jamais ou rarement	☐$_5$ Quotidiennement ☐$_2$ 1 fois/ mois ☐$_4$ 2-3 fois/semaine ☐$_1$ Moins d'une fois/ mois ☐$_3$1 fois/ semaine ☐$_0$ Jamais ou rarement
6. Utilisez-vous une crème pour prévenir les vergetures ? ☐$_0$ Non (allez à Q7) ☐$_1$ Oui ☐$_{99}$ Ne sait pas (allez à Q7)		

Si *oui*	☐5 Quotidiennement	☐2 1 fois/ mois	☐5 Quotidiennement	☐2 1 fois/ mois
	☐4 2-3 fois/semaine	☐1 Moins d'une fois/ mois	☐4 2-3 fois/semaine	☐1 Moins d'une fois/ mois
	☐31 fois/ semaine	☐0 Jamais ou rarement	☐31 fois/ semaine	☐0 Jamais ou rarement

7. Utilisez-vous des parfums ou eaux de cologne ? ☐0 Non (allez à Q8) ☐1 Oui ☐99 Ne sait pas (allez à Q8)

Si *oui*	☐5 Quotidiennement	☐2 1 fois/ mois	☐5 Quotidiennement	☐2 1 fois/ mois
	☐4 2-3 fois/semaine	☐1 Moins d'une fois/ mois	☐4 2-3 fois/semaine	☐1 Moins d'une fois/ mois
	☐31 fois/ semaine	☐0 Jamais ou rarement	☐31 fois/ semaine	☐0 Jamais ou rarement

8. Utilisez-vous des produits de beauté ou produits de soins corporels artisanaux (faits à la main par vous-même, quelqu'un d'autre, non commerciaux) pour un usage sur la peau ou oral ?

☐0 Non ☐1 Oui ☐99 Ne sait pas

9. Quel type de couvre-plancher y a-t-il dans votre maison ? (Cochez toutes les réponses qui s'appliquent)

☐ Bois
☐ Moquette
☐ Plancher flottant
☐ Plancher linoléum
☐ Tuiles en céramique, porcelaine ou ardoise

10. Quand votre maison ou votre appartement a-t-elle/il été contruit(e) ?

☐0 Avant 1960 ☐11960 à 1970 ☐2 1971 à 1980 ☐3 1981 à 1990
☐4 1991 à 2000 ☐5 2001 à 2005 ☐6 Depuis 2006 ☐99 Ne sait pas

11. Depuis combien de temps habitez-vous dans cette maison ou appartement ?

☐0 Moins de 1 an ☐1 1-5 ans ☐2 6-10 ans ☐3 Plus de 10 ans

12. Possédez-vous un écran plat (télé ou ordinateur) de 24 pouces ou plus ?

☐0 Non ☐1 Oui ☐99 Ne sait pas ☐98 Refuse de répondre

12.1. Si ***oui,*** en quelle année avez-vous acheté votre ou vos écran(s) plat(s) ? (*aaaa*)

#1: ☐☐☐☐ #2: ☐☐☐☐ #3: ☐☐☐☐ ☐99 Ne sait pas

13. Pouvez-vous estimer l'origine et la quantité moyenne d'eau que vous avez consommée **par jour durant les 3 derniers mois** (incluant l'eau utilisée pour préparer d'autres breuvages) ?

	0 L	**Moins de 0,5 L**	**0,5 à 1 L**	**1 à 1,5 L**	**Plus de 1,5 L**
Eau du robinet	☐0	☐1	☐2	☐3	☐4
Eau en bouteille en plastique	☐0	☐1	☐2	☐3	☐4
Autre eau (pluie, source, puit)	☐0	☐1	☐2	☐3	☐4
Quantité totale bue par jour	☐0	☐1	☐2	☐3	☐4

14. D'où provient l'eau que vous avez utilisée pour cuisiner **durant les 3 derniers mois** ?

☐0 Robinet ☐1 Bouteille de plastique ☐2 Autre, précisez: _____

15. Si vous buvez l'eau du robinet, d'où provenait cette eau durant les 3 derniers mois ?

☐$_0$ Aqueduc municipal ☐$_1$ Puit privé ☐$_2$ Autre source, précisez : _____ ☐$_{99}$ Ne sait pas

16. Au cours des 3 derniers mois, pouvez-vous estimer quel contact vous avez eu avec l'eau des sources suivantes, sans inclure l'eau utilisée pour cuisiner ou pour boire ?

	Nombre de fois / mois
Douche	☐☐☐
Bain	☐☐☐
Piscine	☐☐☐
Jacuzzi	☐☐☐
Spa	☐☐☐
Sauna	☐☐☐

CARACTÉRISTIQUES SOCIODÉMOGRAPHIQUES

1. Date de naissance *(jj/ mmm/ aaaa)* ☐☐/ ☐☐☐/ ☐☐☐☐

2. Votre code postal ☐☐☐ ☐☐☐

3. Nombre d'années de scolarité complétées ☐☐ ans

3.1. Plus haut niveau de scolarité **atteint**:

☐$_0$ Aucune scolarité

☐$_2$ Primaire terminé

☐$_4$ Secondaire complété

☐$_6$ Cégep, école technique ou d'enseignement, formation collégiale ou formation d'infirmière complétée

☐$_7$ Université 1er cycle ou école d'enseignement complété

☐$_8$ Maîtrise

☐$_9$ Doctorat

☐$_{10}$ Autre ➢ Précisez: _____

☐$_{98}$ Refuse de répondre

4. Les gens au Canada proviennent de divers groupes raciaux ou culturels. Vous appartenez peut-être à plusieurs des groupes suivants. Êtes-vous...*(plusieurs réponses possibles)*

☐ Blanc

☐ Africain

☐ Afro-américain

☐ Latino-américain

☐ Amérindien/ peuple autochtone

☐ Autre, précisez: _____

☐ Asiatique de l'est (e.g. Chinois, Japonais, Vietnamien, Cambodgien, Malaysien, Laotien, Indonésien etc)

☐ Sud-asiatique (e.g. Indien de l'est, Pakistanais, Punjabi, Srilankais, etc)

☐ Arabe/ asiatique occidental (e.g. Arménien, Égyptien, Iranien, Libanais, Marocain)

☐ Ne sait pas

☐ Refuse de répondre

5. Est-ce qu'au moins un de vos parents est d'origine canadienne française? ☐$_0$ Non ☐$_1$ Oui

   ➢ 5.1. Si ***oui,*** veuillez préciser l'origine ethnique de votre :

   Père: _____ Mère: _____

   Grand-mère paternelle:_____ Grand-mère maternelle:_____

   Grand-père paternel: _____ Grand-père maternel: _____

   INTERVIEWER: Veuillez consulter la feuille sur les origines ethniques comme référence.

6. État civil

   ☐$_0$ Mariée
   ☐$_1$ Conjointe de fait ou vivant avec un partenaire
   ☐$_2$ Célibataire (jamais mariée)
   ☐$_3$ Séparée
   ☐$_4$ Divorcée
   ☐$_5$ Veuve
   ☐$_6$ Autre _____

7. Revenu annuel approximatif de votre ménage avant imposition, en **dollars canadiens** *(incluant le revenu de votre partenaire, et d'autres sources de revenu, ex. aide financière de la famille ou des amis) :*

   ☐$_0$ Moins de 10 000
   ☐$_1$ 10 000 – 19 999
   ☐$_2$ 20 000 – 29 999
   ☐$_3$ 30 000 – 39 999
   ☐$_4$ 40 000 – 49999
   ☐$_5$ 50 000 – 59999
   ☐$_6$ 60 000 – 69999
   ☐$_7$ 70 000 – 79999
   ☐$_8$ 80 000 – 99 999
   ☐$_9$ ≥100 000
   ☐$_{99}$ Ne sait pas
   ☐$_{98}$ Refuse de répondre

8. Combien de personnes vivent de ce revenu (incluant les enfants)? ☐☐ personnes

9. Où êtes-vous née ?

   ☐$_0$ Canada ☐$_1$ États-Unis ☐$_2$ Caraïbes ☐$_3$ Océanie ☐$_4$ Afrique
   ☐$_5$ Europe ☐$_6$ Asie ☐$_7$ Mexique, Amérique centrale et Amérique du sud

10. Quelle langue parlez-vous le plus souvent à la maison ?

    ☐ $_0$Anglais ☐$_1$ Français ☐$_2$ Les deux ☐$_3$ Autre ➢ Préciser : _____

11. Quelle est votre langue maternelle (première langue)?
☐0 Anglais ☐1 Français ☐2 Les deux ☐3 Autre ➢ Précisez : _____

MESURES ANTHROPOMÉTRIQUES

1. Poids avant la grossesse ☐☐☐ ☐0 Kg ☐1 livres

2. Poids à cette visite (mesuré) ☐☐☐ ☐0 Kg ☐1 livres

3. Taille à cette visite (mesurée) ☐☐☐ cm *ou* ☐ pieds ☐☐ pouces
   ➢ Si non mesuré ou mesuré indirectement, complétez la SECTION DÉVIATIONS AU PROTOCOLE

MESURE DE LA TENSION ARTÉRIELLE POUR CETTE VISITE (POSITION ASSISE, BRAS GAUCHE)

1. Est-ce que la mesure de la pression sanguine a été effectuée ? ☐0 Non ➢ Complétez la SECTION DÉVIATIONS AU PROTOCOLE ☐1 Oui

➢ Si ***oui***, inscrivez :

1.1. 1re mesure ☐☐☐ / ☐☐☐ mm/Hg
systolique *diastolique*

UNE MINUTE APRÈS

1.2. 2e mesure ☐☐☐ / ☐☐☐ mm/Hg
systolique *diastolique*

SECTION DÉVIATIONS AU PROTOCOLE

1. Y a-t-il eu déviation au protocole relativement aux procédures de cette visite ? ☐$_0$ Non ☐$_1$ Oui
   - Si ***oui,*** précisez :

Visite d'étude	**Précisez la raison**	
☐ 1.1. Visite d'étude faite à l'extérieur de la fenêtre du temps requis ($8^{0/7}$ à $13^{6/7}$)	☐$_0$ Patiente a oublié	☐$_1$ Impossible d'avoir un rendez-vous dans les temps requis
☐ 1.2 Participante non-éligible après inclusion	1.2.1. Précisez : _____	
☐ 1.3 Partie du questionnaire 1A non complétée	1.3.1. Précisez section: _____ 1.3.2. Précisez pages: ☐☐ à ☐☐	
☐ 1.4 Autre	1.4.1. Précisez : _____	
Mesures anthropométriques	**Précisez la raison:**	
☐ 1.5 Poids non mesuré à cette visite	☐$_0$ Infirmière a oublié	☐$_1$ Patiente ne consent pas
	☐$_2$ Poids au dessus de la limite de la balance	
☐ 1.6 Poids obtenu de la participante		
☐ 1.7 Taille non mesurée à cette visite	☐$_0$ Infirmière a oublié	☐$_1$ Patiente ne consent pas
	☐$_2$ Jauge non-disponible	
☐ 1.8 Taille obtenue de la participante		
Mesures de la tension artérielle	**Précisez la raison:**	
☐ 1.9 Mesure de la tension artérielle non effectuée	☐$_0$ Infirmière a oublié	☐$_1$ Patiente ne consent pas
	☐$_2$ Appareil non disponible	

SECTION DE L'INTERVIEWER

1. Initiales ☐☐☐

2. Durée de l'entrevue ☐☐☐ min

3. Signature :_____

4. Date ☐☐/ ☐☐☐/ ☐☐☐☐
(jj/ mmm/ aaaa)

Rappel: les informations concernant la visite d'aujourd'hui doivent être entrées dans la base de données administrative

IRNPQEO Étude 3D

QUESTIONNAIRE 1C – Antécédents obstétricaux

Jour	Mois	Année	Centre	ID	Monogramme
☐☐	☐☐	☐☐☐☐	☐☐	☐☐☐	☐☐☐

Veuillez compléter ce questionnaire pour chaque grossesse précédente, en débutant avec la première grossesse comme numéro 1.

Grossesse numéro : ☐

1. A. Issue de la grossesse :

☐$_0$ Naissance vivante unique ☐$_1$ Naissance vivante multiple ☐$_2$ Mort-né (≥ 20 semaines) ☐$_3$ Naissance(s) vivante(s) et jumeaux mort-né(s) pour une même grossesse multiple

☐$_4$ Avortement induit ☐$_5$ Fausse couche (< 20 semaines) ☐$_6$ Grossesse molaire ☐$_7$ Grossesse ectopique

B. Âge gestationnel à la naissance ou à l'avortement : ☐☐ Semaines ☐ /7 jours

Si naissance à moins de 37 semaines, précisez la prématurité :

☐$_0$ Spontanée ☐$_1$ Décision du personnel medical ☐$_2$ Après une rupture prématurée des membranes

C. Type d'accouchement ☐$_0$ Césarienne ☐$_1$ Vaginal ☐$_{97}$ Ne s'applique pas

D. Caractéristiques des bébés (si > 20 semaines)

	Sexe	**Poids**	**Toujours vivant**
Bébé 1	☐$_0$ Masculin ☐$_1$ Féminin ☐$_2$ Indéterminé	☐☐ lbs ☐☐ oz **ou** ☐☐☐☐ grammes	☐$_0$ Non ☐$_1$ Oui
Bébé 2 ☐ N/A	☐$_0$ Masculin ☐$_1$ Féminin ☐$_2$ Indéterminé	☐☐ lbs ☐☐ oz **ou** ☐☐☐☐ grammes	☐$_0$ Non ☐$_1$ Oui
Bébé 3 ☐ N/A	☐$_0$ Masculin ☐$_1$ Féminin ☐$_2$ Indéterminé	☐☐ lbs ☐☐ oz **ou** ☐☐☐☐ grammes	☐$_0$ Non ☐$_1$ Oui

2. Avez-vous donné naissance à un enfant ayant des malformations congénitales dans le cadre de cette grossesse ?

☐$_0$ Non ☐$_1$ Oui ➢ Précisez la malformation _____ ☐$_{97}$ N/A

3. Avez-vous eu une interruption de grossesse planifiée pour cause d'anomalie fœtale ?

☐$_0$ Non ☐$_1$ Oui ➢ Précisez l'anomalie fœtale _____ ☐$_{97}$ N/A

4. Avez-vous eu l'un des problèmes suivants durant cette grossesse ?

☐$_0$ Non ➢ Continuez à la question 5. ☐$_1$ Oui ➢ Indiquez ci-dessous les problèmes importants

	Non	**Oui**	**Ne sait pas**
Cerclage	☐$_0$	☐$_1$	☐$_{99}$
Pré-éclampsie/ Éclampsie (incluant syndrome HELLP)	☐$_0$	☐$_1$	☐$_{99}$
Hypertension gravidique (sans PE)	☐$_0$	☐$_1$	☐$_{99}$
Diabète gestationnel	☐$_0$	☐$_1$	☐$_{99}$
Placenta praevia	☐$_0$	☐$_1$	☐$_{99}$
Hématome rétroplacentaire	☐$_0$	☐$_1$	☐$_{99}$
Autre ➢ Précisez : _____	☐$_0$	☐$_1$	☐$_{99}$

5. Aviez-vous le même partenaire lors de cette grossesse qu'à l'heure actuelle ?

☐$_0$ Non ☐$_1$ Oui

IRNPQEO Étude 3D

QUESTIONNAIRE 2B – Questionnaire maternel visite 2

Web/autoadministré (entre 20 0/7 et 24 6/7 semaines)

Jour	Mois	Année	Centre	ID	Monogramme

SECTION STRESS ET HUMEUR

Les questions suivantes portent sur des événements qui pourraient avoir eu lieu **depuis que vous êtes enceinte**. Pour chacun des événements, veuillez indiquer à quel point cet événement était négatif, indésirable ou difficile en utilisant l'échelle appropriée.

1. **Depuis que vous êtes enceinte**, avez-vous déménagé ou cherché un nouveau logement?
   ☐ Non ☐ Oui ☐ Ne sait pas ☐ Refuse de répondre

   1.1 **Si oui**, jusqu'à quel point cet événement était-il négatif ou indésirable?

   ☐Pas du tout ☐ Un peu ☐Modérément ☐Beaucoup

2. **Depuis que vous êtes enceinte**, est-ce que quelqu'un est venu vivre avec vous ?
   ☐ Non ☐ Oui ☐ Ne sait pas ☐ Refuse de répondre

   2.1 **Si oui**, jusqu'à quel point cet événement était-il négatif ou indésirable?

   ☐Pas du tout ☐ Un peu ☐Modérément ☐Beaucoup

3. **Depuis que vous êtes enceinte**, avez-vous vécu loin de votre mari ou conjoint à cause de son travail, de voyages ou d'autres raisons pratiques comme cela?
   ☐ Non ☐ Oui ☐ Ne sait pas ☐ Refuse de répondre

   3.1 **Si oui**, jusqu'à quel point cet événement était-il négatif ou indésirable?

   ☐Pas du tout ☐ Un peu ☐Modérément ☐Beaucoup

4. **Depuis que vous êtes enceinte**, vous êtes-vous mariée ou avez-vous commencé à vivre avec quelqu'un (comme si vous étiez mariés) ?
   ☐ Non ☐ Oui ☐ Ne sait pas ☐ Refuse de répondre

   4.1 **Si oui**, jusqu'à quel point cet événement était-il négatif ou indésirable?

   ☐Pas du tout ☐ Un peu ☐Modérément ☐Beaucoup

5. **Depuis que vous êtes enceinte**, avez-vous eu un surplus de responsabilités à la maison tel que devoir prendre soin d'une personne âgée de la famille ou de l'enfant de quelqu'un d'autre ?
☐ Non ☐ Oui ☐ Ne sait pas ☐ Refuse de répondre

5.1 **Si oui**, jusqu'à quel point cet événement était-il négatif ou indésirable?

☐Pas du tout ☐ Un peu ☐Modérément ☐Beaucoup

6. **Depuis que vous êtes enceinte**, avez-vous été cambriolée ou volée ?
☐ Non ☐ Oui ☐ Ne sait pas ☐ Refuse de répondre

6.1 **Si oui**, jusqu'à quel point cet événement était-il négatif ou indésirable?

☐Pas du tout ☐ Un peu ☐Modérément ☐Beaucoup

7. **Depuis que vous êtes enceinte**, avez-vous perdu votre maison, votre auto ou quelque chose d'important pour vous ?
☐ Non ☐ Oui ☐ Ne sait pas ☐ Refuse de répondre

7.1 **Si oui**, jusqu'à quel point cet événement était-il négatif ou indésirable?

☐Pas du tout ☐ Un peu ☐Modérément ☐Beaucoup

8. **Depuis que vous êtes enceinte**, est-ce que quelqu'un qui était proche de vous et important pour vous est décédé ?
☐ Non ☐ Oui ☐ Ne sait pas ☐ Refuse de répondre

Si oui, 8.1 Quel est le lien avec cette personne: _____

8.2 Jusqu'à quel point cet événement était-il négatif ou indésirable?

☐Pas du tout ☐ Un peu ☐Modérément ☐Beaucoup

9. **Depuis que vous êtes enceinte**, avez-vous vécu l'expérience d'un feu, d'une inondation ou d'un autre désastre majeur?
☐ Non ☐ Oui ☐ Ne sait pas ☐ Refuse de répondre

9.1 **Si oui,** jusqu'à quel point cet événement était-il négatif ou indésirable?

☐Pas du tout ☐ Un peu ☐Modérément ☐Beaucoup

10. **Depuis que vous êtes enceinte**, avez-vous subi de la discrimination à cause de votre origine ethnique, de votre race ou de votre religion?
☐ Non ☐ Oui ☐ Ne sait pas ☐ Refuse de répondre

10.1 **Si oui,** jusqu'à quel point cet événement était-il négatif ou indésirable?

☐Pas du tout ☐ Un peu ☐Modérément ☐Beaucoup

11. **Depuis que vous êtes enceinte**, avez-vous été impliquée dans un accident de véhicule motorisé sérieux ?

☐ Non ☐ Oui ☐ Ne sait pas ☐ Refuse de répondre

11.1 **Si oui,** jusqu'à quel point cet événement était-il négatif ou indésirable?

☐Pas du tout ☐ Un peu ☐Modérément ☐Beaucoup

12. **Depuis que vous êtes enceinte**, avez-vous eu des problèmes avec l'assistance sociale?
☐ Non ☐ Oui ☐ Ne sait pas ☐ Refuse de répondre

12.1 **Si oui,** jusqu'à quel point cet événement était-il négatif ou indésirable?

☐Pas du tout ☐ Un peu ☐Modérément ☐Beaucoup

13. **Depuis que vous êtes enceinte**, avez-vous été séparée de votre mari (conjoint) parce que vous ne vous entendiez pas bien ensemble?
☐ Non ☐ Oui ☐ Ne sait pas ☐ Refuse de répondre

13.1 **Si oui,** jusqu'à quel point cet événement était-il négatif ou indésirable?

☐Pas du tout ☐ Un peu ☐Modérément ☐Beaucoup

14. **Depuis que vous êtes enceinte** avez-vous eu un divorce ou une séparation?
☐ Non ☐ Oui ☐ Ne sait pas ☐ Refuse de répondre

14.1 **Si oui,** jusqu'à quel point cet événement était-il négatif ou indésirable?

☐Pas du tout ☐ Un peu ☐Modérément ☐Beaucoup

15. **Depuis que vous êtes enceinte**, un autre événement important vous est-il arrivé?
☐ Non ☐ Oui ☐ Ne sait pas ☐ Refuse de répondre

Si oui, 15.1 Veuillez préciser: _____

15.2 Jusqu'à quel point cet événement était-il négatif ou indésirable?

☐Pas du tout ☐ Un peu ☐Modérément ☐Beaucoup

16. **Depuis que vous êtes enceinte**, avez-vous, (ou un membre de votre famille ou un ami), été arrêté par la police, eu des problèmes avec la loi ou l'immigration ou été en prison ?
☐ Non ☐ Oui ☐ Ne sait pas ☐ Refuse de répondre

Si oui, pour qui et jusqu'à quel point cet événement était-il négatif ou indésirable?

Qui?	**Non**	**Oui**	**Jusqu'à quel point cet événement était-il négatif ou indésirable?**			
16.1 Vous	☐	☐	☐Pas du tout	☐ Un peu	☐Modérément	☐ Beaucoup

16.2 Membre de votre famille	☐	☐	☐Pas du tout	☐ Un peu	☐ Modérément	☐ Beaucoup
16.3 Ami(e) proche	☐	☐	☐Pas du tout	☐ Un peu	☐Modérément	☐ Beaucoup
16.4 Autre	☐	☐	☐$_0$Pas du tout	☐$_1$ Un peu	☐$_2$ Modérément	☐$_3$ Beaucoup
16.1.4.1Si autre, préciser:			_____			

17. **Depuis que vous êtes enceinte,** avez-vous eu ou un membre de votre famille ou un(e) ami(e), a-t-il eu une maladie, été blessé sérieusement ou été hospitalisé ?
☐ Non ☐ Oui ☐ Ne sait pas ☐ Refuse de répondre

Si oui, pour qui et jusqu'à quel point cet événement était-il négatif ou indésirable?

Qui?	**Non**	**Oui**	**Jusqu'à quel point cet événement était-il négatif ou indésirable?**			
17.1 Vous	☐	☐	☐Pas du tout	☐ Un peu	☐Modérément	☐ Beaucoup
17.2 Membre de votre famille	☐	☐	☐Pas du tout	☐ Un peu	☐Modérément	☐ Beaucoup
17.3 Ami(e) proche	☐	☐	☐Pas du tout	☐ Un peu	☐Modérément	☐ Beaucoup
17.4 Autre	☐	☐	☐Pas du tout	☐ Un peu	☐Modérément	☐ Beaucoup
Si autre, préciser			_____			

Les questions suivantes portent sur vos sentiments et vos pensées **au cours des 7 derniers jours.** Pour chaque question, veuillez indiquer avec quelle fréquence vous vous êtes sentie ainsi, selon l'échelle suivante: jamais, rarement, parfois, assez souvent, très souvent.

	Jamais	Rarement	Parfois	Assez souvent	Très souvent
18. **Au cours des 7 derniers jours**, combien de fois avez-vous ressenti que vous étiez incapable de contrôler les aspects importants de votre vie ?	☐	☐	☐	☐	☐
19. **Au cours des 7 derniers jours**, combien de fois vous êtes-vous sentie confiante en votre capacité de régler vos problèmes personnels ?	☐	☐	☐	☐	☐
20. **Au cours des 7 derniers jours**, combien de fois avez-vous ressenti que les choses allaient comme vous le vouliez ?	☐	☐	☐	☐	☐
21. **Au cours des 7 derniers jours**, combien de fois avez-vous ressenti que les difficultés se multipliaient au point où vous vous sentiez incapable de les surmonter? [	☐	☐	☐	☐	☐

Pour chaque question, veuillez indiquer avec quelle fréquence vous vous êtes sentie ainsi, selon l'échelle suivante: jamais, rarement, parfois, assez souvent, presque toujours.

	Jamais	Rarement	Parfois	Assez souvent	Presque toujours
22. **Au cours des 7 derniers jours**, combien de fois le fait d'être enceinte vous a-t-il fait sentir nerveuse ?	☐	☐	☐	☐	☐
23. **Au cours des 7 derniers jours**, combien de fois vous êtes-vous sentie préoccupée par le fait d'être enceinte ?	☐	☐	☐	☐	☐
24. **Au cours des 7 derniers jours**, combien de fois le fait d'être enceinte vous a-t-il fait peur?	☐	☐	☐	☐	☐
25. **Au cours des 7 derniers jours**, combien de fois vous êtes-vous sentie paniquée par le fait d'être enceinte ?	☐	☐	☐	☐	☐

26. Avez-vous un mari / conjoint? ☐ Non ➢ Passez à la question 28 ☐Oui

Les questions qui suivent portent sur des attitudes et des comportements de votre couple. Même dans les couples qui vont bien, il peut y avoir des tensions, des difficultés ou des conflits.

27. Les énoncés suivants correspondent à différents degrés de bonheur dans votre relation de couple. Veuillez inscrire, tout compte fait, le chiffre qui correspond le mieux au degré de bonheur de votre couple. Au centre, " heureuse " correspond au degré de bonheur retrouvé dans la plupart des relations de couple. L'échelle augmente graduellement vers la droite pour les rares personnes qui connaissent un bonheur parfait dans leur relation de couple et elle diminue vers la gauche pour celles qui sont très malheureuses.

☐ Ne sait pas

1---------- 2 ---------- 3 ---------- 4 ---------- 5 ---------- 6---------- 7 ☐ Refuse de répondre

Très malheureuse — Heureuse — Très heureuse

Veuillez indiquer à quel point vous êtes en accord ou en désaccord avec les affirmations en utilisant l'échelle suivante : Fortement en désaccord, en désaccord, ni en accord ni en désaccord, en accord, ou fortement en accord.

a) Propositions	**Fortement en désaccord**	**En désaccord**	**Ni en accord ni en désaccord**	**En accord**	**Fortement en accord**	**Refuse de répondre**	**Ne sait pas**
28. En période d'incertitude, en général, je m'attends au mieux.	☐	☐	☐	☐	☐	☐	☐
29. S'il y a une possibilité que quelque chose aille mal pour moi, cela arrivera.	☐	☐	☐	☐	☐	☐	☐
30. Je vois toujours le bon côté des choses.	☐	☐	☐	☐	☐	☐	☐
31. Je suis toujours optimiste au sujet de mon avenir.	☐	☐	☐	☐	☐	☐	☐
32. Je ne m'attends presque jamais à ce que les choses aillent en ma faveur.	☐	☐	☐	☐	☐	☐	☐
33. Les choses ne vont jamais comme je le veux.	☐	☐	☐	☐	☐	☐	☐
34. Je crois que " toute chose a son bon côté ".	☐	☐	☐	☐	☐	☐	☐
35. Je m'attends rarement à ce que de bonnes choses m'arrivent.	☐	☐	☐	☐	☐	☐	☐

	Tout à fait en désaccord	**Plutôt en désaccord**	**Plutôt en accord**	**Tout à fait en accord**	**Refuse de répondre**	**Ne sait pas**
36. J'ai une attitude positive vis-à-vis moi-même.	☐	☐	☐	☐	☐	☐
37. Dans l'ensemble, je suis satisfaite de moi	☐	☐	☐	☐	☐	☐
38. Parfois je me sens vraiment inutile.	☐	☐	☐	☐	☐	☐
39. Il m'arrive de penser que je suis une bonne à rien.	☐	☐	☐	☐	☐	☐

Les questions suivantes portent sur vos sentiments à propos de vos relations avec votre entourage. Nous aimerions savoir comment cela se passe en général dans vos relations avec les gens et pas seulement à propos d'une relation en particulier. Veuillez indiquer jusqu'à quel point vous êtes en désaccord ou en accord avec chacune des affirmations suivantes en utilisant l'échelle correspondante.

40. Je m'inquiète beaucoup au sujet de mes relations avec les gens. ☐ Ne sait pas

1---------- 2 ---------- 3 ---------- 4 ---------- 5 ---------- 6---------- 7 ☐ Refuse de répondre

Tout à fait en désaccord — Tout à fait d'accord

41. Je préfère ne pas montrer aux autres comment je me sens en-dedans. ☐ Ne sait pas

1---------- 2 ---------- 3 ---------- 4 ---------- 5 ---------- 6---------- 7 ☐ Refuse de répondre

Tout à fait en désaccord — Tout à fait d'accord

42. Je me sens à l'aise de dépendre des autres. ☐ Ne sait pas

1---------- 2 ---------- 3 ---------- 4 ---------- 5 ---------- 6---------- 7 ☐ Refuse de répondre

Tout à fait en désaccord — Tout à fait d'accord

43. Je m'inquiète d'être abandonnée. ☐ Ne sait pas

1---------- 2 ---------- 3 ---------- 4 ---------- 5 ---------- 6---------- 7 ☐ Refuse de répondre

Tout à fait en désaccord — Tout à fait d'accord

44. Je me sens très à l'aise d'être intime avec d'autres. ☐ Ne sait pas

1---------- 2 ---------- 3 ---------- 4 ---------- 5 ---------- 6---------- 7 ☐ Refuse de répondre

Tout à fait en désaccord — Tout à fait d'accord

45. Je trouve cela difficile de me permettre de dépendre des autres ☐ Ne sait pas

1---------- 2 ---------- 3 ---------- 4 ---------- 5 ---------- 6---------- 7 ☐ Refuse de répondre

Tout à fait en désaccord — Tout à fait d'accord

Voici maintenant une série d'affirmations qui décrivent comment vous avez pu vous sentir ou ce qui vous est arrivé **au cours de la dernière semaine.** Veuillez indiquer la fréquence avec laquelle ces situations se sont appliquées à vous **au cours de la dernière semaine** en cochant la case appropriée.

	Très rarement (< 1 jour/ semaine)	**Occasion-nellement** (1 à 2 jours / semaine)	**Assez souvent** (3 à 4 jours / semaine)	**Fréquemment, tout le temps** (5 à 7 jours / semaine)	**Refuse de répondre**
46. J'ai eu l'impression que je ne pouvais pas me remonter le moral même avec l'aide de ma famille ou de mes amis.	☐	☐	☐	☐	☐
47. Je me suis sentie déprimée.	☐	☐	☐	☐	☐
48. Je me suis sentie seule.	☐	☐	☐	☐	☐
49. Je me suis sentie triste.	☐	☐	☐	☐	☐

	Jamais	**Rarement**	**Parfois**	**Souvent**	**Constam-ment**
50. Vous arrive-t-il d'avoir très peur et d'éviter certains endroits (par exemple: ascenseurs, avions, hauteurs, eau), animaux (par exemple : chiens, insectes, araignées) ou situations impliquant du sang ou des interventions médicales ou dentaires?	☐	☐	☐	☐	☐
51. Vous arrive-t-il d'être très anxieuse dans certaines situations sociales et de les éviter parce que vous avez peur de faire une gaffe ou d'être jugée par d'autres personnes? Ces situations peuvent impliquer de commencer ou de continuer une conversation, de manger ou d'écrire en public, de parler devant un groupe, etc.	☐	☐	☐	☐	☐
52. Vous arrive-t-il de ressentir une montée soudaine et imprévisible de craintes ou de malaises intenses (la montée peut être caractérisée par des palpitations, le souffle coupé, une douleur thoracique, des étourdissements, la peur de mourir, etc.)?	☐	☐	☐	☐	☐
53. Vous arrive-t-il d'éviter certaines situations par peur de ne pas être capable de sortir ou de ne pas obtenir de l'aide si vous ressentez des symptômes comme la diarrhée, des vomissements, des étourdissements ou une attaque de panique?	☐	☐	☐	☐	☐
54. Vous arrive-t-il de ressentir des tensions musculaires, d'être agitée ou de vous sentir fébrile lorsque vous êtes inquiète?	☐	☐	☐	☐	☐

55.	Vous arrive-t-il de vous inquiéter excessivement ou d'une façon exagérée au point que vous trouviez cela difficile de contrôler vos inquiétudes?	☐	☐	☐	☐	☐
56.	Vous arrive-t-il d'être dérangée par des pensées, des images ou des impulsions qui reviennent sans cesse et qui peuvent vous sembler inappropriées, bizarres ou absurdes, mais contre lesquelles vous ne pouvez rien?	☐	☐	☐	☐	☐
57.	Vous arrive-t-il de vous sentir obligée de répéter le même comportement (par exemple : laver, vérifier, ordonner, ranger, etc.) ou la même idée maintes et maintes fois afin de contrôler une pensée, prévenir un malheur, soulager un sentiment de malaise?	☐	☐	☐	☐	☐
58.	Votre vie quotidienne est-elle affectée par des souvenirs, des rêves ou d'autres signes de détresse par rapport à un événement que vous avez vécu ou dont vous avez été témoin et qui était traumatisant ou mettait votre vie ou celles d'autres personnes en danger?	☐	☐	☐	☐	☐
59.	Vous arrive-t-il d'être fortement préoccupée par l'idée que vous êtes atteinte d'une maladie grave malgré un bilan médical rassurant?	☐	☐	☐	☐	☐

60. À quel point l'une ou l'autre des manifestations décrites aux questions 50 à 59, vous empêche-t-elle de bien fonctionner dans une ou plusieurs parties de votre vie, c'est-à-dire dans votre travail, vos activités sociales, votre famille, etc.?

☐ Aucunement ☐ Légèrement ☐ Modérément ☐ Sévèrement ☐ Totalement

SECTION ACTIVITÉ PHYSIQUE

DEPUIS VOTRE DERNIÈRE VISITE

Il est très important que vous répondiez honnêtement aux questions. Il n'y a pas de bonne ou de mauvaise réponse. Nous voulons seulement connaître les choses que vous faisiez **depuis votre dernière visite**.

Depuis votre dernière visite, quand vous **N'ÉTIEZ PAS** au travail, combien de temps passiez-vous généralement à.

1. Préparer les repas (cuisiner, mettre la table, laver la vaisselle)
   - ☐ Jamais
   - ☐ Moins de1/2 h/ jour
   - ☐ 1/2 h à presque 1h/ jour
   - ☐ 1h à presque 2h/ jour
   - ☐ 2h à presque 3h/ jour
   - ☐ 3 heures ou plus/ jour

2. Habiller, laver et nourrir les enfants en étant **assise**
   - ☐ Jamais
   - ☐ Moins de1/2 h/ jour
   - ☐ 1/2 h à presque 1h/ jour
   - ☐ 1h à presque 2h/ jour
   - ☐ 2h à presque 3h/ jour
   - ☐ 3 heures ou plus/ jour

3. Habiller, laver et nourrir les enfants en étant **debout**
   - ☐ Jamais
   - ☐ Moins de1/2 h/ jour
   - ☐ 1/2 h à presque 1h/ jour
   - ☐ 1h à presque 2h/ jour
   - ☐ 2h à presque 3h/ jour
   - ☐ 3 heures ou plus/ jour

4. Jouer avec les enfants en étant **assise** ou **debout**
   - ☐ Jamais
   - ☐ Moins de1/2 h/ jour
   - ☐ 1/2 h à presque 1h/ jour
   - ☐ 1h à presque 2h/ jour
   - ☐ 2h à presque 3h/ jour
   - ☐ 3 heures ou plus/ jour

5. Jouer avec les enfants en **marchant** ou **courant**
   - ☐ Jamais
   - ☐ Moins de1/2 h/ jour
   - ☐ 1/2 h à presque 1h/ jour
   - ☐ 1h à presque 2h/ jour
   - ☐ 2h à presque 3h/ jour
   - ☐ 3 heures ou plus/ jour

6. Porter des enfants (dans les bras, porte-bébé, sur le dos, etc.)
   - ☐ Jamais
   - ☐ Moins de1/2 h/ jour
   - ☐ 1/2 h à presque 1h/ jour
   - ☐ 1h à presque 2h/ jour
   - ☐ 2h à presque 3h/ jour
   - ☐ 3 heures ou plus/ jour

7. Prendre soin d'une personne âgée

- ☐ Jamais
- ☐ Moins de1/2 h/ jour
- ☐ 1/2 h à presque 1h/ jour
- ☐ 1h à presque 2h/ jour
- ☐ 2h à presque 3h/ jour
- ☐ 3 heures ou plus/ jour

8. Vous asseoir pour utiliser un ordinateur ou écrire lorsque vous n'êtes **pas** au travail

- ☐ Jamais
- ☐ Moins de1/2 h/ jour
- ☐ 1/2 h à presque 1h/ jour
- ☐ 1h à presque 2h/ jour
- ☐ 2h à presque 3h/ jour
- ☐ 3 heures ou plus/ jour

9. Regarder la télévision, une vidéo ou un DVD

- ☐ Jamais
- ☐ Moins de1/2 h/ jour
- ☐ 1/2 h à presque 2 h/ jour
- ☐ 2 h à presque 4 h/ jour
- ☐ 4 h à presque 6 h/ jour
- ☐ 6 heures ou plus/ jour

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10. Vous asseoir pour lire, parler ou téléphoner, lorsque vous n'êtes **pas** au travail

- ☐ Jamais
- ☐ Moins de1/2 h/ jour
- ☐ 1/2 h à presque 2 h/ jour
- ☐ 2 h à presque 4 h/ jour
- ☐ 4 h à presque 6 h/ jour
- ☐ 6 heures ou plus/ jour

11. Jouer avec des animaux domestiques

- ☐ Jamais
- ☐ Moins de1/2 h/ jour
- ☐ 1/2 h à presque 1h/ jour
- ☐ 1h à presque 2h/ jour
- ☐ 2h à presque 3h/ jour
- ☐ 3 heures ou plus/ jour

12. Faire les tâches ménagères habituelles (faire les lits, la lessive, repasser, ranger les choses)

- ☐ Jamais
- ☐ Moins de1/2 h/ jour
- ☐ 1/2 h à presque 1h/ jour
- ☐ 1h à presque 2h/ jour
- ☐ 2h à presque 3h/ jour
- ☐ 3 heures ou plus/ jour

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13. Magasiner (nourriture, vêtements, ou autres items)

- ☐ Jamais
- ☐ Moins de1/2 h/ jour
- ☐ 1/2 h à presque 1h/ jour
- ☐ 1h à presque 2h/ jour
- ☐ 2h à presque 3h/ jour
- ☐ 3 heures ou plus/ jour

14. Faire le ménage (passer l'aspirateur, passer la vadrouille, balayer, laver les fenêtres)

- ☐ Jamais
- ☐ Moins de1/2 h/ semaine
- ☐ 1/2 h à presque 1h/ semaine
- ☐ 1h à presque 2h/ semaine
- ☐ 2h à presque 3h/ semaine
- ☐ 3 heures ou plus/ semaine

15. Tondre la pelouse à l'aide d'un tracteur à pelouse (position assise)

- ☐ Jamais
- ☐ Moins de1/2 h/ semaine
- ☐ 1/2 h à presque 1h/ semaine
- ☐ 1h à presque 2h/ semaine
- ☐ 2h à presque 3h/ semaine
- ☐ 3 heures ou plus/ semaine

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16. Tondre la pelouse à l'aide d'une tondeuse à gazon (debout), râteler les feuilles, jardiner ou pelleter la neige

- ☐ Jamais

☐ Moins de1/2 h/ semaine

☐ 1/2 h à presque 1h/ semaine

☐ 1h à presque 2h/ semaine

☐ 2h à presque 3h/ semaine

☐ 3 heures ou plus/ semaine

DÉPLACEMENTS

Depuis votre dernière visite, combien de temps passiez-vous généralement à...

17. Marcher **lentement** pour vous déplacer à un endroit (par exemple : pour prendre l'autobus, aller au travail, rendre visite), et **pas** pour le plaisir ou l'exercice
    ☐ Jamais
    ☐ Moins de1/2 h/ jour
    ☐ 1/2 h à presque 1h/ jour
    ☐ 1h à presque 2h/ jour
    ☐ 2h à presque 3h/ jour
    ☐ 3 heures ou plus/ jour

18. Marcher **rapidement** pour vous rendre à un endroit (par exemple : pour prendre l'autobus, aller au travail ou à l'école), et **pas** pour le plaisir ou l'exercice
    ☐ Jamais
    ☐ Moins de1/2 h/ jour
    ☐ 1/2 h à presque 1h/ jour
    ☐ 1h à presque 2h/ jour
    ☐ 2h à presque 3h/ jour
    ☐ 3 heures ou plus/ jour

19. Conduire ou prendre place dans une voiture ou un autobus
    ☐ Jamais
    ☐ Moins de1/2 h/ jour
    ☐ 1/2 h à presque 1h/ jour
    ☐ 1h à presque 2h/ jour
    ☐ 2h à presque 3h/ jour
    ☐ 3 heures ou plus/ jour

POUR LE PLAISIR OU L'EXERCICE

Depuis votre dernière visite, combien de temps passiez-vous généralement à...

20. Marcher **lentement** pour le plaisir ou comme exercice
- ☐ Jamais
- ☐ Moins de1/2 h/ semaine
- ☐ 1/2 h à presque 1h/ semaine
- ☐ 1h à presque 2h/ semaine
- ☐ 2h à presque 3h/ semaine
- ☐ 3 heures ou plus/ semaine

21. Marcher **rapidement** pour le plaisir ou comme exercice
- ☐ Jamais
- ☐ Moins de1/2 h/ semaine
- ☐ 1/2 h à presque 1h/ semaine
- ☐ 1h à presque 2h/ semaine
- ☐ 2h à presque 3h/ semaine
- ☐ 3 heures ou plus/ semaine

22. Marcher **rapidement en montée** pour le plaisir ou comme exercice
- ☐ Jamais
- ☐ Moins de1/2 h/ semaine
- ☐ 1/2 h à presque 1h/ semaine
- ☐ 1h à presque 2h/ semaine
- ☐ 2h à presque 3h/ semaine
- ☐ 3 heures ou plus/ semaine

23. Jogger
- ☐ Jamais
- ☐ Moins de1/2 h/ semaine
- ☐ 1/2 h à presque 1h/ semaine
- ☐ 1h à presque 2h/ semaine
- ☐ 2h à presque 3h/ semaine
- ☐ 3 heures ou plus/ semaine

24. Suivre des cours d'exercices prénataux
- ☐ Jamais
- ☐ Moins de1/2 h/ semaine
- ☐ 1/2 h à presque 1h/ semaine
- ☐ 1h à presque 2h/ semaine
- ☐ 2h à presque 3h/ semaine
- ☐ 3 heures ou plus/ semaine

25. Nager
- ☐ Jamais
- ☐ Moins de1/2 h/ semaine
- ☐ 1/2 h à presque 1h/ semaine
- ☐ 1h à presque 2h/ semaine
- ☐ 2h à presque 3h/ semaine
- ☐ 3 heures ou plus/ semaine

26. Danser
- ☐ Jamais
- ☐ Moins de1/2 h/ semaine
- ☐ 1/2 h à presque 1h/ semaine
- ☐ 1h à presque 2h/ semaine
- ☐ 2h à presque 3h/ semaine
- ☐ 3 heures ou plus/ semaine

Avez-vous fait autre(s) chose(s) pour le plaisir ou comme exercice ?

☐ Je n'ai pas fait autre chose pour le plaisir ou comme exercice.

☐ J'ai fait une activité pour le plaisir ou comme exercice. ➢ Complétez la question 27

☐ J'ai fait deux activités pour le plaisir ou comme exercice. ➢ Complétez les questions 27 et 28

S'il-vous-plaît, à l'aide de la liste d'exemples dans le menu «Aide» :

- **Nommez cette activité. Si cette activité entre dans la catégorie «Autres», nommez-la tout de même.**
- **Sélectionnez la catégorie dans laquelle apparaît cette activité dans la liste déroulante ci-dessous.**
- **Cochez le temps passé sur cette activité.**

27. Nom de l'activité : _____
Catégorie : Musculation

Temps passé sur l'activité :

☐ Jamais
☐ Moins de1/2 h/ semaine
☐ 1/2 h à presque 1h/ semaine
☐ 1h à presque 2h/ semaine
☐ 2h à presque 3h/ semaine
☐ 3 heures ou plus/ semaine

28. Nom de l'activité : _____
Catégorie : Musculation

Temps passé sur l'activité :

☐ Jamais
☐ Moins de1/2 h/ semaine
☐ 1/2 h à presque 1h/ semaine
☐ 1h à presque 2h/ semaine
☐ 2h à presque 3h/ semaine
☐ 3 heures ou plus/ semaine

AU TRAVAIL

S'il vous plaît, complétez la prochaine section si, **depuis votre dernière visite**, vous travailliez avec rémunération, comme bénévole ou si vous étiez étudiante. Si vous étiez femme au foyer, sans emploi ou dans l'incapacité de travailler, vous n'avez pas besoin de remplir cette section.

Depuis votre dernière visite, combien de temps passiez-vous généralement à :

29. Être assise pendant le travail ou en classe

- ☐ Jamais
- ☐ Moins de1/2 h/ jour
- ☐ 1/2 h à presque 2h/ jour
- ☐ 2h à presque 4h/ jour
- ☐ 4h à presque 6h/ jour
- ☐ 6h ou plus/ jour

30. Être debout ou marcher **lentement** pendant le travail tout en transportant des choses plus lourdes qu'un gallon (4 litres) de lait

- ☐ Jamais
- ☐ Moins de1/2 h/ jour
- ☐ 1/2 h à presque 2h/ jour
- ☐ 2h à presque 4h/ jour
- ☐ 4h à presque 6h/ jour
- ☐ 6h ou plus/ jour

31. Être debout ou marcher **lentement** pendant le travail **sans** transporter quoi que ce soit

- ☐ Jamais
- ☐ Moins de1/2 h/ jour
- ☐ 1/2 h à presque 2h/ jour
- ☐ 2h à presque 4h/ jour
- ☐ 4h à presque 6h/ jour
- ☐ 6h ou plus/ jour

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32. Marcher **rapidement** pendant le travail tout en transportant des choses plus lourdes qu'un gallon (4 litres) de lait

- ☐ Jamais
- ☐ Moins de1/2 h/ jour
- ☐ 1/2 h à presque 2h/ jour
- ☐ 2h à presque 4h/ jour
- ☐ 4h à presque 6h/ jour
- ☐ 6h ou plus/ jour

33. Marcher **rapidement** pendant le travail sans transporter quoi que ce soit

- ☐ Jamais
- ☐ Moins de1/2 h/ jour
- ☐ 1/2 h à presque 2h/ jour
- ☐ 2h à presque 4h/ jour
- ☐ 4h à presque 6h/ jour
- ☐ 6h ou plus/ jour

SECTION SUR LE SOMMEIL

Les questions suivantes font référence à vos habitudes de sommeil **DU DERNIER MOIS**. Vos réponses devraient correspondre aux meilleures estimations possibles pour la **majorité** des jours et des nuits du dernier mois. Veuillez répondre à toutes les questions.

1. **Durant le dernier mois**, à quelle heure vous êtes-vous couchée les soirs de semaine? Heure habituelle du coucher : ☐☐h ☐☐min

2. **Durant le dernier mois**, combien de temps (en min.) avez-vous pris pour vous endormir à chaque soir ? ☐☐min

3. **Durant le dernier mois**, à quelle heure vous êtes-vous levée le matin? Heure habituelle du lever : ☐☐h ☐☐min

4. **Durant le dernier mois**, combien d'heures de sommeil avez-vous eues par nuit ? ☐☐h

   - *Ceci peut être différent du nombre d'heures passées au lit*

Pour chacune des questions suivantes, cochez la meilleure réponse. S.V.P. répondez à toutes les questions.

5. **Durant le dernier mois**, combien de fois avez-vous eu de la difficulté à dormir parce que vous...

		Pas durant le dernier mois	Moins d'une fois par semaine	1 à 2 fois par semaine	3 fois ou plus par semaine	Ne sait pas
5.1	Ne pouviez pas vous endormir à l'intérieur de 30 minutes ?	☐	☐	☐	☐	☐
5.2	Vous réveilliez au milieu de la nuit ou tôt le matin ?	☐	☐	☐	☐	☐
5.3	Deviez-vous lever pour aller à la salle de bain ?	☐	☐	☐	☐	☐
5.4	Ne pouviez pas respirer facilement ?	☐	☐	☐	☐	☐
5.5	Toussiez ou ronfliez bruyamment ?	☐	☐	☐	☐	☐
5.6	Aviez trop froid ?	☐	☐	☐	☐	☐
5.7	Aviez trop chaud ?	☐	☐	☐	☐	☐
5.8	Aviez fait de mauvais rêves ?	☐	☐	☐	☐	☐
5.9	Ressentiez de la douleur ?	☐	☐	☐	☐	☐
5.10	Autre(s) raison(s) Veuillez préciser : _____	☐	☐	☐	☐	☐

6. **Durant le dernier mois**, comment évalueriez-vous la qualité globale de votre sommeil ?

☐ Très bien ☐ Plutôt bien ☐ Plutôt mal ☐ Très mal

7. **Durant le dernier mois**, combien de fois avez-vous pris une médication (avec ou sans ordonnance) pour vous aider à dormir ?

☐ Pas durant le dernier mois ☐ Moins d'une fois par semaine ☐ 1 ou 2 fois par semaine ☐ 3 fois ou plus par semaine

8. **Durant le dernier mois**, combien de fois avez-vous eu de la difficulté à rester éveillée pendant que vous conduisiez, mangiez ou vous engagiez dans une activité sociale ?

☐ Pas durant le dernier mois ☐ Moins d'une fois par semaine ☐ 1 ou 2 fois par semaine ☐ 3 fois ou plus par semaine

9. **Durant le dernier mois**, jusqu'à quel point avez-vous eu de la difficulté à maintenir suffisamment d'enthousiasme pour compléter vos activités ?

☐ Aucune difficulté ☐ Légère difficulté ☐ Quelque peu de difficulté ☐ Beaucoup de difficulté

10. Avez-vous un partenaire de lit ou de chambre?

☐ Pas de partenaire de lit ou co-locataire de chambre ☐ Partenaire ou colocataire dans une autre chambre ☐ Partenaire dans la même chambre mais pas le même lit ☐ Partenaire dans le même lit

➢ Allez à Q 11

Si vous avez un partenaire de lit ou de chambre, **DEMANDEZ-LUI** combien de fois **dans le dernier mois** vous avez...

	Pas durant le dernier mois	Moins d'une fois par semaine	1 à 2 fois par semaine	3 fois ou plus par semaine	Ne sait pas
10.1 Ronflé bruyamment?	☐	☐	☐	☐	☐
10.2 Eu de longues pauses entre les respirations pendant votre sommeil ?	☐	☐	☐	☐	☐
10.3 Eu des contractions ou des secousses dans les jambes pendant votre sommeil ?	☐	☐	☐	☐	☐
10.4 Eu des épisodes de désorientation ou de confusion durant le sommeil ?	☐	☐	☐	☐	☐
10.5 Eu d'autres agitations pendant que vous dormiez ? Veuillez préciser : _____	☐	☐	☐	☐	☐

11. **Durant le dernier mois**, combien de jours par semaine avez-vous fait une sieste de 5 minutes ou plus ?

☐Jamais ➢ Allez à la section suivante ☐1 ou 2 jours par semaine 3 à 5 jours par semaine ☐6 jours ou plus par semaine

12. Lorsque vous faites une sieste, combien de temps dormez-vous ?

☐☐h ☐☐min

<u>À PROPOS DE L'INSÉCURITÉ ALIMENTAIRE</u>

À cause des taux élevés de chômage et de la grande difficulté à trouver du travail, de plus en plus de familles éprouvent de la difficulté à joindre les deux bouts et il arrive que la nourriture vienne à manquer. Nous voudrions savoir si quelque chose de semblable a pu vous arriver.

1. **Depuis votre dernière visite,** est-il déjà arrivé que vous n'ayez pas mangé suffisamment parce que votre famille était à court de nourriture et que vous n'aviez plus d'argent pour en acheter ?

☐Non ➢Fin du questionnaire ☐Oui ➢ Répondez à Q1.1

1.1 À quelle fréquence avez-vous manqué de nourriture **depuis votre dernière visite ?**

☐ Régulièrement, à chaque mois

☐ Plus d'une fois par mois

☐ Certains mois seulement

☐ Occasionnellement, mais pas régulièrement

☐ Refuse de répondre

IRNPQEO Étude 3D

QUESTIONNAIRE 5B – Questionnaire révision du dossier pour grossesses ≥ 20 semaines

Jour	Mois	Année	Centre	ID	Monogramme
☐☐	☐☐☐	☐☐☐☐	☐☐	☐☐☐	☐☐☐

Veuillez compléter ce questionnaire selon **les informations contenues dans le dossier clinique de la participante.** N'oubliez pas d'inscrire tous les médicaments indiqués dans le dossier dans le questionnaire MML.

SECTION TOLÉRANCE AU GLUCOSE DURANT LA GROSSESSE

1. Est-ce qu'une épreuve de charge en glucose (50 g) a été réalisée durant cette grossesse ?

   ☐$_0$ Non ➢Allez à Q2 ☐$_1$ Oui ➢Précisez

   1.2. Date *(jj/ mmm/ aaaa)* ☐☐/ ☐☐☐/ **20**☐☐

   1.3. Résultat ☐☐☐mg/dL ou ☐.☐ mmol/L

2. Est-ce qu'une épreuve de tolérance au glucose (OGTT)a été réalisée durant cette grossesse?

   ☐$_0$ Non ➢Allez à Q3 ☐$_1$ 75 g ☐$_2$ 100 g

   2.1. Date *(jj/ mmm/ aaaa)* ☐☐/ ☐☐☐/ **20**☐☐

   2.2. Résultats

   2.2.1. À jeun ☐☐☐ mg/dL ou ☐.☐ mmol/L

   2.2.2. 1 heure ☐☐☐ mg/dL ou ☐.☐ mmol/L

   2.2.3. 2 heures ☐☐☐ mg/dL ou ☐.☐ mmol/L

   2.2.4. 3 heures (100 g seulement) ☐☐☐ mg/dL ou ☐.☐ mmol/L

3. Diabète gestationnel

   ☐$_0$ Non ☐$_1$ Oui ➢Précisez

3.1. Date du diagnostic *(jj/ mmm/ aaaa)* ☐☐/ ☐☐☐/ **20**☐☐

SECTION CORTICOSTEROÏDES DURANT LA GROSSESSE

5. La participante a-t'elle reçu des corticostéroïdes pour prévention de la maladie des membranes hyalines néonatale (= maladie respiratoire) durant sa grossesse ?

☐$_0$ Non ➢Allez à la SECTION PRESSION SANGUINE ET ANALYSE D'URINE ☐$_1$ Oui ➢Précisez

1.1. Combien de doses a-t-elle reçues ?

☐$_0$ Une seule dose de 12 mg de bétamethasone

☐$_1$ Une seule série (2 x 12 mg de bétamethasone en 24 h)

☐$_2$ Dose(s) additionnelles (2 doses de12 mg de bétamethasone par semaine aux 24 h, jusqu'à la 34ième semaine de gestation ou la naissance)

Si dose(s) additionnelle(s), combien ? ☐☐

☐$_3$ Autre ➢ Précisez : _____

1.2. Combien de temps avant l'accouchement la participante a-t-elle reçu sa dernière dose ?

☐$_0$ < 24 h ☐$_1$ ≥ 24 h mais < 7 jours ☐$_2$ ≥ 7 jours

SECTION TENSION ARTÉRIELLE ET ANALYSE D'URINE

1. Plus haute mesure de tension artérielle **avant** l'admission pour l'accouchement ☐☐☐/☐☐☐ mm/Hg

Systolique/Diastolique

1.1. Date *(jj/ mmm/ aaaa)* ☐☐/ ☐☐☐/ **20**☐☐ 1.2. Heure (sur 24h) ☐☐ h ☐☐ min

2. Le diagnostic d'hypertension gravidique a-t-il été posé par le médecin de la participante **avant** son admission pour l'accouchement (après 20 semaines) ?

☐$_0$ Non ☐$_1$ Oui ➢Précisez

2.1. Date du premier diagnostic *(jj/ mmm/ aaaa)* ☐☐/ ☐☐☐/ **20**☐☐

3. Une analyse d'urine par bâtonnet réactif a-t-elle été faite **avant l'admission pour accouchement** ?

☐$_0$ Non ☐$_1$ Oui ➢Précisez

3.1. Indiquer le **résultat le plus élevé** pour les protéines

☐$_0$ Négatif ☐$_2$ 30 mg/dL ou 0.3 g/L ☐$_4$ 300 mg/dL ou 3.0 g/L

☐$_1$ Trace ☐$_3$ 100 mg/dL ou 1.0 g/L ☐$_5$ ≥2000 mg/dL ou ≥20 g/L

4. Une collecte d'urine pendant 24 heures a-t-elle était faite **avant l'admission pour accouchement** ?

☐$_0$ Non ☐$_1$ Oui ➢Précisez

4.1. Indiquer le **résultat le plus élevé** de protéinurie obtenu ☐☐☐☐☐ mg/24h **ou** ☐☐.☐ g/L

4.2 Un ratio créatinine/protéine fut-il effectué? ☐$_0$ Non ☐$_1$ Oui

5. Plus haute mesure de pression artérielle diastolique **après** l'admission pour l'accouchement

5.1. ☐☐☐/☐☐☐ mm/Hg

Systolique/Diastolique

5.2. Date *(j/j mmm/ aaaa)* ☐☐/ ☐☐☐/ **20**☐☐

5.3. Heure (sur 24h) ☐☐ h ☐☐ min

6. Inscrivez la mesure suivante, prise **≥ 4 heures plus tard**

6.1. ☐☐☐/☐☐☐ mm/Hg

Systolique/Diastolique

6.2. Date *(jj/ mmm/ aaaa)* ☐☐/ ☐☐☐/ **20**☐☐

6.3. Heure (sur 24h) ☐☐ h ☐☐ min

7. Le diagnostic d'hypertension gravidique a-t-il été posé par le médecin **au cours de ou après** l'admission pour accouchement ?

☐0 Non ☐1 Oui

8. La participante a-t-elle reçu un agent antihypertensif **après** son admission pour accouchement ?

☐0 Non ☐1 Oui

9. Une analyse d'urine pour protéine par bâtonnet réactif a-t-elle été faite **après l'admission** ?

☐0 Non ☐1 Oui ➢Précisez

9.1. Indiquez le **résultat le plus élevé** de protéinurie obtenu

☐0 Négatif ☐2 30 mg/dL ou 0.3 g/L ☐4 300 mg/dL ou 3.0 g/L

☐1 Trace ☐3 100 mg/dL ou 1.0 g/L ☐5 ≥2000 mg/dL ou ≥ 20 g/L

10. Une collecte d'urine pendant 24 heures a-t-elle était faite **après l'admission** ?

☐0 Non ☐1 Oui ➢Précisez

10.1. Indiquez le résultat de protéinurie obtenu ☐☐☐☐☐ mg/24h **ou** ☐☐.☐ g/L

10.2 Un ratio créatinine/protéine fut-il effectué? ☐0 Non ☐1 Oui

SECTION ANALYSES CLINIQUES DES TESTS PRÉNATAUX DE LABORATOIRE

Si disponible au dossier de la participante.
Si le test a été fait plus d'une fois, inscrire le résultat du premier test. (*Veuillez porter une **attention particulière aux unités**.)*

Test	Fait	Résultat	Date *(jj/ mmm/ aaaa)*
1. Hémoglobine	☐0 Non ☐1 Oui	☐☐☐ g/L ou ☐☐.☐ g/dL	☐☐/ ☐☐☐/ **20**☐☐
2. Férritine sérique	☐0 Non ☐1 Oui	☐☐☐ng/mL ou ☐☐☐ µg/L	☐☐/ ☐☐☐/ **20**☐☐
3. TSH:	☐0 Non ☐1 Oui	☐.☐☐mU/L	☐☐/ ☐☐☐/ **20**☐☐
4. Hormone thyroidienne T4	☐0 Non ☐1 Oui	☐☐☐mg/L ou ☐☐☐ nmol/L	☐☐/ ☐☐☐/ **20**☐☐
5. Hormone thyroidienne T4 libre (FT4)	☐0 Non ☐1 Oui	____ mg/L ou ☐☐.☐☐ pmol/L	☐☐/ ☐☐☐/ **20**☐☐
6. Hormone thyroidienne T3	☐0 Non ☐1 Oui	____ mg/L ou☐.☐nmol/L	☐☐/ ☐☐☐/ **20**☐☐
7. Dépistage prénatal pour Trisomie 21 (Syndrome de Down) ?	☐0 Non ☐1 Oui	➢ Si oui, complétez 7.1 à 7.6 ➢ Si non, passez à la SECTION MESURES ANTHROPOMÉTRIQUES AVANT L'ACCOUCHEMENT	

Test	Fait	Résultat	Date *(jj/ mmm/ aaaa)*
7.1 hCG libre	☐0 Non ☐1 Oui	_____MoMs	☐☐/ ☐☐☐/ 20☐☐
7.2. hCG totale	☐0 Non ☐1 Oui	_____MoMs ou ☐☐☐.☐☐ IU/L	☐☐/ ☐☐☐/ 20☐☐
7.3. PAPP-A	☐0 Non ☐1 Oui	_____MoMs ou ☐.☐☐ IU/L	☐☐/ ☐☐☐/ 20☐☐
7.4. AFP	☐0 Non ☐1 Oui	_____MoMs ou ☐☐.☐☐ IU/mL	☐☐/ ☐☐☐/ 20☐☐
7.5. Inhibine	☐0 Non ☐1 Oui	_____MoMs ou ☐☐☐.☐☐ pg/mL	☐☐/ ☐☐☐/ 20☐☐
7.6. Estriol	☐0 Non ☐1 Oui	_____MoMs ou ☐.☐☐ nmol/L	☐☐/ ☐☐☐/ 20☐☐

SECTION MESURE ANTHROPOMÉTRIQUE AVANT L'ACCOUCHEMENT

1. Dernier poids maternel mesuré avant l'accouchement ☐☐☐.☐ ☐0 kg **ou** ☐1 lbs

2. Date de la pesée *(jj/ mmm/ aaaa)* ☐☐/ ☐☐☐/ 20☐☐

SECTION TRAVAIL ET ACCOUCHEMENT

1. Admission pour accouchement

1.1. Date *(jj/ mmm/ aaaa)* ☐☐/ ☐☐☐/ 20☐☐

1.2. Heure (sur 24h) ☐☐ h ☐☐ min

2. La patiente a-t-elle débuté son travail ? (Note : « L'induction » n'inclut pas la stimulation d'un travail déjà en cours par oxytocine)

☐0 Non ☐1 Spontané ➢ Complétez les questions 2.1 et 2.2 ☐2 Induit ➢ Complétez les questions 2.3 à 2.5

2.1 Date de début *(jj/ mmm/ aaaa)* ☐☐/ ☐☐☐/ 20☐☐

2.2 Heure de début (sur 24 h) ☐☐ h ☐☐ min

2.3 Méthode de maturation du col ☐0 Non ☐1 Oui ➢Précisez

2.3.1 Si oui, précisez (plusieurs réponses possibles)

Mécanique

☐0 Ballonnet de Foley

Pharmacologique

☐2 Cervidil

☐$_1$ Tiges laminaires ☐$_3$ Prépidil

☐$_4$ Prostin

☐$_5$ Autre ➢ Précisez:_____

2.4 Méthode d'induction (plusieurs réponses possibles)

☐ Oxytocine ☐ Rupture artificielle des membranes ☐ Misoprostol

☐ Prostin ☐ Autre ➢ Précisez:_____

2.5 Heure du début de l'induction (sur 24h) ☐☐ h ☐☐ min

3. Rupture des membranes ☐$_0$ Spontanée ☐$_1$ Artificielle

3.1. Date de la rupture *(jj/ mmm/ aaaa)* ☐☐/ ☐☐☐/ **20**☐☐

3.2. Heure de la rupture (sur 24h) ☐☐ h ☐☐ min

5. Type d'anesthésie

☐$_0$ Aucune ☐$_1$ Locale ☐$_2$ Épidurale ☐$_3$ Rachianesthésie ☐$_4$ Générale ☐$_5$ Blocage du nerf honteux ☐$_6$ Autre

6. Prophylaxie antibiotique?

☐$_0$ Non ☐$_1$ Oui

NAISSANCE DU BÉBÉ

7. Date *(jj/ mmm/ aaaa)* ☐☐/ ☐☐☐/ **20**☐☐

8. Heure (sur 24 h) ☐☐ h ☐☐ min

9. Présentation du bébé

☐$_0$ Céphalique ☐$_1$ Siège ☐$_2$ Autre

10. Poids du placenta ☐☐☐☐ g

11. Fièvre maternelle durant le travail (≥38C) ☐$_0$ Non ☐$_1$ Oui

12. Estimé du sang perdu pendant l'accouchement (ml) ☐$_0$ < 500 ☐$_1$ 500-900 ☐$_2$ 1000-1499 ☐$_3$ ≥ 1500

13. Type d'accouchement

☐$_0$ Spontané ☐$_1$ Césarienne ➢ Précisez ☐$_2$ Vaginal – ventouse ☐$_3$ Vaginal - forceps

Si ***césarienne***, précisez l'(les) indication(s) : (plusieurs réponses possibles)

☐ Dystocie ☐ Mauvaise présentation ☐ Suspicion de souffrance fœtale basée sur un tracé anormal

☐ Saignements ☐ Suspicion de macrosomie ☐ Pathologie hypertensive sévère (incluant pré-éclampsie)

☐ Placenta abruptio ☐ Placenta praevia ☐ Échec de ventouse ou de forceps

☐ Échec d'induction ☐ Antécédent de césarienne ☐ Demande maternelle

☐ Autre : _____

14. Abruptio Placentae

☐$_0$ Non ☐$_1$ Oui

15. Monitorage fœtal intra partum (plus d'une réponse possible)

☐ Aucun ☐ Monitoring fœtal électronique continu (ECG) ☐ Oxymétrie du pouls foetal

☐ Biochimie sanguine foetale (pH cuir chevelu) ☐ Auscultation intermittente

CONDITION MATERNELLE AVANT ET APRÈS L'ADMISSION POUR ACCOUCHEMENT

La répondante a-t-elle présenté l'une ou l'autre des conditions suivantes **avant ou après** son admission pour accouchement ?

1. Convulsions – éclampsie ☐$_0$ Non ☐$_1$ Oui ➢Précisez

   1.1. Date de la première convulsion (*jj/ mmm/ aaaa*) ☐☐/ ☐☐☐/ **20**☐☐

2. Hausse importante de la tension artérielle **diastolique** (≥110 mmHg) ? ☐$_0$ Non ☐$_1$ Oui

3. Hausse importante de la tension artérielle **systolique** (≥ 160 mmHg) ? ☐$_0$ Non ☐$_1$ Oui

4. Hématocrite < 24.0% ☐$_0$ Non ☐$_1$ Oui ☐$_2$ Non fait

5. Transfusion ☐$_0$ Non ☐$_1$ Oui

6. Hospitalisation avant l'accouchement ☐$_0$ Non ☐$_1$ Oui ➢Précisez

6.1. ➢ Précisez l'(les) indication(s) : 6.1.1 _____

6.1.2 _____

6.1.3 _____

6.2. Nombre de fois admise à l'hôpital ☐☐ fois

6.3. Nombre total de jours d'hospitalisation avant l'admission pour accouchement ☐☐ jours

7. Infection maternelle (autre que chorioamnionite) ☐$_0$ Non ☐$_1$ Oui ➢Précisez

7.1. Précisez laquelle: _____

8. Dépistage du Streptocoque B effectué ? ☐$_0$ Non ☐$_1$ Oui ➢Précisez

8.1. Précisez le résultat : _____

9. Fièvre maternelle après l'accouchement
(≥38.5°C, minimum à 2 reprises à plus de 24 heures d'intervalle, excluant les 24 premières heures après l'accouchement)

☐$_0$ Non ☐$_1$ Oui

10. Infection maternelle ☐$_0$ Non ☐$_1$ Oui ➢ Précisez (plusieurs réponses possibles)

☐ Endométrite ☐ Infection de l'épisiotomie ☐ Infection de la cicatrice abdominale ☐ Infection des voies urinaires

☐ Autre ➢ Précisez: _____

11. La participante a-t-elle eu <u>un ou plusieurs des problèmes suivants</u> avant son congé ou son transfert ?
☐$_0$ Non ☐$_1$ Oui ➢Précisez (plusieurs réponses possibles)

☐ Hémorragie ante partum nécessitant un accouchement en urgence

☐ Coagulation intravasculaire disséminée

☐ Œdème pulmonaire

☐ Admission en Unité de Soins Intensifs ➢ Précisez 11.1. Durée ☐☐ jour(s) ☐☐ heures

11.2 Diagnostic principal : _____

☐ Hystérectomie

☐ Rupture utérine

☐ Collapsus cardio respiratoire

☐ Transfusion ➢ Précisez la quantité: ☐☐☐☐ ml

☐ Décès ➢ Précisez la cause première du décès: _____

☐ Autre complication maternelle ➢ Précisez: _____

12. La participante a-t-elle été transférée dans un autre hôpital ? ☐$_0$ Non ☐$_1$ Oui ➢ Précisez

12.1. Nom de l'hôpital : _____

12.2. Raison du transfert : _____

13. Date et heure du congé/transfert de l'hôpital ou a eu lieu l'accouchement (ou le décès)

13.1. Date *(jj/ mmm/ aaaa)* ☐☐/ ☐☐☐/ **20**☐☐ 13.2. Heure (sur24h) : ☐☐ h ☐☐min

SECTION HISTOPATHOLOGIE

1. Une analyse histopathologique du placenta a-t-elle était faite ?

☐$_0$ Non ☐$_1$ Oui ➢Précisez ☐$_{99}$ Ne sait pas

1.1. Inscrivez les résultats : _____

_____

SECTION INFORMATION NÉONATALE BÉBÉ

1. Poids à la naissance ☐☐☐☐ g
2. Taille à la naissance ☐☐.☐ cm
3. Périmètre crânien ☐☐.☐ cm
4. Sexe ☐$_0$ M ☐$_1$ F ☐$_2$ Inconnu
5. Âge gestationnel à la naissance ☐☐ semaines ☐ jours/7

6. Le bébé présente-t-il une (des) anomalie(s) congénitale(s) ? ☐$_0$ Non ☐$_1$ Oui ➢Précisez

6.1. Inscrivez le code CDC de cette/ces anomalie(s)

☐☐☐.☐☐☐ ☐☐☐.☐☐☐ ☐☐☐.☐☐☐ ☐☐☐.☐☐☐

6.2. Le karyotpye a-t-il été analysé ? ☐$_0$ Non ☐$_1$ Oui ➢Précisez

6.2.1. Précisez les résultats_____

6.3 Une analyse CGH a-t-elle été effectuée? ☐$_0$ Non ☐$_1$ Oui ➢Précisez

6.3.1. Précisez les résultats_____

7. Le bébé est-il né vivant?

☐$_0$ Non ➢ Allez à la question 8 ☐$_1$ Oui➢ Allez à la question 7.1

7.1 Le bébé est-il décédé à l'hôpital de naissance ?

☐$_0$ Non ➢ Allez à la question 10 ☐$_1$ Oui

8. Précisez la date du décès : *(jj/mmm/aaaa)* ☐☐/ ☐☐☐/ **20**☐☐

9. Y a-t-il eu autopsie ?

☐$_0$ Non➢ Allez à la question 9.3 ☐$_1$ Oui ➢ Complétez les questions 9.1 et 9.2

9.1. Quelle était la cause première du décès selon l'autopsie ?

☐$_0$ Prématurité ☐$_1$ RCIU sévère ☐$_2$ Malformation congénitale ☐$_3$ Asphyxie

☐$_4$ Septicémie ☐$_5$ Trauma à la naissance ☐$_6$ Autre

9.2. Précisez toute autre cause particulière qui aurait pu contribuer au décès selon l'autopise

_____

9.3. Précisez la cause première du décès

_____

9.4. Précisez toute autre cause du décès

_____

Si le bébé n'était pas vivant à la naissance, arrêtez la collecte des données et complétez la SECTION DÉVIATION DU PROTOCOLE

10. Score Apgar

10.1. ☐☐ 1 min ☐ non fait 10.2. ☐☐ 5 min ☐ non fait 10.3. ☐☐ 10 min ☐ non fait

	Indéter-miné	Artère	Non fait	Veine	Non fait
11. pH ombilical du bébé	☐	☐.☐☐	☐	☐.☐☐	☐
12. Excès/déficit de base ombilical du bébé	☐	☐☐.☐ ☐0 Positif ☐1 Négatif	☐	☐☐.☐ ☐0 Positif ☐1 Négatif	☐

13. Le bébé a-t-il été admis en Unité Néonatale de Soins Intensifs ?

☐0 Non ➢ Allez à question 14 ☐1 Oui ➢ Complétez le QUESTIONNAIRE 5D

13.1. Durée du séjour ☐☐ jours ☐☐ heures

13.2. Diagnostic à l'admission _____

14. Le bébé a-t-il reçu des antibiotiques par voie systémique ? ☐0 Non ☐1 Oui ➢ Précisez

14.1. Pour quelle raison ont-ils été prescrits ? _____

15. Le bébé avait-il une septicémie soupçonée ou confirmée? ☐0 Non ☐1 Oui

16. Une ou plusieurs hémoculture(s) a(ont)-t-elle(s) été faite(s) ? ☐0 Non ☐1 Oui ➢ Précisez

16.1. Résultat des cultures ☐0 Négatif ☐1 Positif

17. Une ponction lombaire a-t-elle été faite ? ☐0 Non ☐1 Oui

17.1. Résultat de la culture: ☐0 Négatif ☐1 Positif

18. Le bébé présente-il un traumatisme lié à la naissance ? ☐0 Non ☐1 Oui ➢Précisez :

☐ Paralysie faciale ☐ Paralysie brachiale ☐ Fracture de la clavicule ☐ Fracture du crâne ☐ Hémorragie sous-galéale

☐ Lacérations cutanées ☐ Blessure de la colonne vertébrale ☐ Blessure des organes internes (foie, rate, etc.) ☐ Céphalohématome

19. Le bébé a-t-il présenté une hypoglycémie (moins de 2.7 mmol/L) dans les premières 24 heures après la naissance ?

☐$_0$ Non ☐$_1$ Oui

21. Le bébé a-t-il présenté une hyperbilirubinémie ? ☐$_0$ Non ☐$_1$ Oui ➢ Précisez

21.1. Valeur de bilirubine la plus élevée : ☐☐.☐ µmol/L

21.2. La photothérapie a-t-elle été nécessaire ? ☐$_0$ Non ☐$_1$ Oui

22. Le bébé a-t-il présenté une détresse respiratoire néonatale? ☐$_0$ Non ☐$_1$ Oui ➢ Précisez

22.1 Le bébé a-t-il reçu un ou plusieurs des traitements suivants? (plusieurs réponses possibles)

☐ Oxygénothérapie ☐ Ventilation assistée non invasive ☐ Ventilation assistée invasive

23. Le bébé a-t-il subi une opération avant son congé ? ☐$_0$ Non ☐$_1$ Oui ➢ Précisez

23.1. Précisez la raison de la chirurgie _____

23.2. Quelle était l'intervention chirurgicale ? _____

24. Autre problème d'ordre médical ☐$_0$ Non ☐$_1$ Oui

24.1. Précisez : _____

25. Le bébé a-t-il été transféré à un autre hôpital ?

☐$_0$ Non ☐$_1$ Oui ➢ Complétez le QUESTIONNAIRE 5D pour bébés transférés ou admis au soins intensifs néonataux

25.1. Nom de l'hôpital :

☐$_1$CHU HSJ ☐$_3$RVH ☐$_4$ CHUQ ☐$_5$ CHUS ☐$_8$ JGH ☐$_9$ HMR ☐$_0$ Children's

☐$_{15}$ Other: _____

25.2. Indiquer la raison du transfert : _____

26. Date et heure du transfert/ congé de l'hôpital de naissance (ou décès)

26.1. Date *(jj/ mmm/ aaaa)* ☐☐/ ☐☐☐/ ☐☐☐☐

26.2. Heure (sur 24 h) ☐☐ h ☐☐ min

SECTION DÉVIATIONS AU PROTOCOLE

1. Y a t-il eu des déviations au protocole pour cette visite ? ☐$_0$ Non ☐$_1$ Oui ➢Précisez

Précisez la raison

1.1. ☐ Revue de dossier non complétée ☐$_0$ Dossier non disponible ☐$_1$ Information manquante ☐$_2$ Parent/ participante ne consent pas

1.2. ☐$_0$ Partie du questionnaire 5B non-complétée 1.3.3. Précisez section: _____

1.3.4. Précisez pages: ☐☐ à ☐☐

SECTION DE L'INTERVIEWER

1. Initiales ☐☐☐

2. Durée de révision ☐☐☐ min

3. Signature de l'interviewer : _____ 4. Date *(jj/ mmm/ aaaa)* ☐☐/ ☐☐☐/ ☐☐☐☐

Rappel: les informations concernant la visite d'aujourd'hui doivent être entrées dans le registre des visites